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1	45801	urinary or bladder or dysuria	USPAT; US-PGPUB	2003/06/27 20:36
2	836	(acetylcholinesterase or 'ACHE') with inhibitor	USPAT; US-PGPUB	2003/06/27 20:37
3	102	(urinary or bladder or dysuria) and ((acetylcholinesterase or 'ACHE') with inhibitor)	USPAT; US-PGPUB	2003/06/27 20:37

EAST

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09/ 960,477

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NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
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NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
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NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
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NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA
NEWS 41	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 42	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 43	Jun 06	PASCAL enhanced with additional data
NEWS 44	Jun 20	2003 edition of the FSTA Thesaurus is now available

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NEWS 45 Jun 25 HSDB has been reloaded

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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=> s (acetylcholinesterase or cholinesterase) and (urinary or bladder or incontinence or dysuria)
19691 ACETYLCHOLINESTERASE
20728 CHOLINESTERASE
111501 URINARY
26068 BLADDER
2264 INCONTINENCE
155 DYSURIA
L1 387 (ACETYLCHOLINESTERASE OR CHOLINESTERASE) AND (URINARY OR BLADDER OR INCONTINENCE OR DYSURIA)

09/ 960,477

=> s l1 and pyrrolo
7532 PYRROLO
L2 2 L1 AND PYRROLO

=> d l2 1- ibib abs
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L2 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:907186 CAPLUS
DOCUMENT NUMBER: 138:350
TITLE: Agents and crystals for improving excretory potency of **urinary bladder**
INVENTOR(S): Ishihara, Yuji; Doi, Takayuki; Nagabukuro, Hiroshi; Ishichi, Yuji
PATENT ASSIGNEE(S): Japan
SOURCE: U.S. Pat. Appl. Publ., 65 pp., Cont.-in-part of U. S. Ser. No. 787,288.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002177593	A1	20021128	US 2001-960477	20010924
WO 2000018391	A1	20000406	WO 1999-JP5367	19990930
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2001335576	A2	20011204	JP 2001-85190	20010323

PRIORITY APPLN. INFO.:
JP 1998-276677 A 19980930
WO 1999-JP5367 W 19990930
US 2001-787288 A2 20010315
JP 2001-85190 A 20010323
JP 2000-88523 A 20000324

OTHER SOURCE(S): MARPAT 138:350
AB Agents for improving potency of the **urinary bladder** which comprises an amine compd. of non-carbamate-type having an **acetylcholinesterase**-inhibiting action. Particularly, crystals of a tricyclic, condensed, heterocyclic deriv. are provided, which possess an excellent action to inhibit **acetylcholinesterase** and an action to improve the excretory potency of **urinary bladder**. As an example, crystals of 8-[3-[1-[(3-fluorophenyl)-methyl]-4-piperidinyl]-1-oxopropyl]-1,2,5,6-tetrahydro-4H-**pyrrolo**[3,2,1-ij]quinolin-4-one or a salt thereof and pharmaceutical compns. contg. them are disclosed.

L2 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:873241 CAPLUS
DOCUMENT NUMBER: 136:15242
TITLE: Crystals of condensed heterotricycle as **acetylcholinesterase** inhibitor and pharmaceutical compositions containing the crystals
INVENTOR(S): Ishihara, Yuji; Doi, Takayuki; Ishiji, Yuji
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 50 pp.
CODEN: JKXXAF

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DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001335576	A2	20011204	JP 2001-85190	20010323
US 2002177593	A1	20021128	US 2001-960477	20010924

PRIORITY APPLN. INFO.:

JP 2000-88523	A	20000324
JP 1998-276677	A	19980930
WO 1999-JP5367	W	19990930
US 2001-787288	A2	20010315
JP 2001-85190	A	20010323

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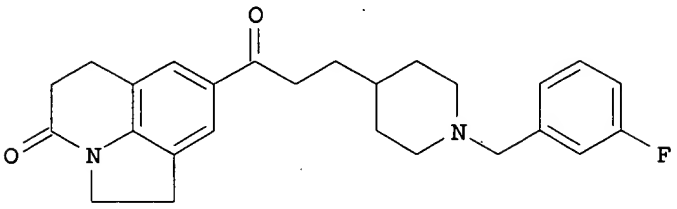

I

AB Crystals of 8-[3-[1-[(3-fluorophenyl)methyl]-4-piperidinyl]-1-oxopropyl]-1,2,5,6-tetrahydro-4H-**pyrrolo**[3,2,1-ij]quinolin-4-one (I) or its salts, preferably having m.p. 113-118.degree., and pharmaceutical compns. contg. the crystals are claimed. The compns. are useful for treatment of **dysuria** by increasing force of **bladder** emptying. The crystals may be used in combination with .alpha.-blockers. Thus, crude crystal of I (prepn. given) was dissolved in AcOEt/MeOH/CHCl3 and the soln. was subjected to silica gel chromatog. After repeating the process, the crystal was dissolved in EtOH and the soln. was heated to remove EtOH and cooled under stirring for 6 h to give I having m.p. 114-117.degree..

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     (FILE 'HOME' ENTERED AT 17:48:50 ON 27 JUN 2003)

     FILE 'CAPLUS' ENTERED AT 17:49:18 ON 27 JUN 2003
L1           387 S (ACETYLCHOLINESTERASE OR CHOLINESTERASE) AND (URINARY OR BLAD
L2             2 S L1 AND PYRROLO

=> s l1 not l2
L3           385 L1 NOT L2

=> s l3 not py>1998
       4146905 PY>1998
L4           345 L3 NOT PY>1998

=> s l4 and (tricyclic or tricycle?)
         15416 TRICYCLIC
          1383 TRICYCLE?
L5              1 L4 AND (TRICYCLIC OR TRICYCLE?)

=> d l5 1 ibib abs

L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:        1997:617007  CAPLUS
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09/ 960,477

DOCUMENT NUMBER: 127:288186
TITLE: Methods of treating neurological diseases and etiologically related symptomology using carbonyl trapping agents in combination with previously known medicaments
INVENTOR(S): Shapiro, Howard K.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 37 pp., Cont.-in-part of U.S. Ser. No. 26,617, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5668117	A	19970916	US 1993-62201	19930629
CA 2166383	AA	19950112	CA 1994-2166383	19940628
WO 9501096	A1	19950112	WO 1994-US7277	19940628
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9472144	A1	19950124	AU 1994-72144	19940628
AU 692454	B2	19980611		
EP 707446	A1	19960424	EP 1994-921405	19940628
R: DE, FR, GB, IT				
JP 08512055	T2	19961217	JP 1994-503597	19940628

PRIORITY APPLN. INFO.: US 1991-660561 B1 19910222
US 1993-26617 B2 19930223
US 1993-62201 A 19930629
WO 1994-US7277 W 19940628
OTHER SOURCE(S): MARPAT 127:288186
AB Therapeutic compns. comprising an effective amt. of at least one carbonyl trapping agent alone or in combination with a therapeutically effective of a co-agent or medicament are disclosed. The compns. are used to treat a mammal suffering from a neurol. disease characterized by covalent bond crosslinking between the nerve cells, other cellular structures and their intracellular and extracellular components, with disease-induced carbonyl-contg. aliph. or arom. hydrocarbons present in mammals.

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(FILE 'HOME' ENTERED AT 17:48:50 ON 27 JUN 2003)

FILE 'CAPLUS' ENTERED AT 17:49:18 ON 27 JUN 2003
L1 387 S (ACETYLCHOLINESTERASE OR CHOLINESTERASE) AND (URINARY OR BLAD
L2 2 S L1 AND PYRROLO
L3 385 S L1 NOT L2
L4 345 S L3 NOT PY>1998
L5 1 S L4 AND (TRICYCLIC OR TRICYCLE?)

=> s l4 not l5
L6 344 L4 NOT L5

=> s l6 not py>1997
4943032 PY>1997
L7 328 L6 NOT PY>1997

=> d l7 1-20 ibib abs

L7 ANSWER 1 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:125445 CAPLUS

DOCUMENT NUMBER: 128:144546
TITLE: Clinical-radiological evaluation of acute pulmonary edema due to exposure to organophosphorus pesticides
AUTHOR(S): Bray, A.; Bianco, P.; Meduri, A.; Pirronti, T.
CORPORATE SOURCE: Universita Cattolica del S. Cuore, Roma-Instituto di Radiologia, Italy
SOURCE: Archivio di Scienze del Lavoro (1995), 11(3), 135-138
CODEN: ASLAEH; ISSN: 0394-2953
PUBLISHER: Istituto Poligrafico e Zecca dello Stato
DOCUMENT TYPE: Journal
LANGUAGE: Italian
AB We report a case of acute poisoning in a farmer with occupational exposure to organophosphorus pesticides. The toxic action of these compds. occurs when they conjugate with **cholinesterase** enzymes in the body, thereby inactivating them. As a consequence, the subject displays evident cholinergic symptoms including flushing of the skin and excess sweating, tachycardia and a fall in blood pressure, increased intestinal movements with colic and diarrhea, **urinary incontinence**, miosis of the eye, bronchoconstriction and profuse bronchial secretion. We analyze the development and the radioligand evolution of pulmonary edema in accidental poisoning due to occupational exposure to organophosphorus pesticides in a farmer.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:120769 CAPLUS
DOCUMENT NUMBER: 128:177110
TITLE: Surveillance of occupational, accidental, and incidental exposure to organophosphate pesticides using urine alkyl phosphate and phenolic metabolite measurements
AUTHOR(S): Davies, John E.; Peterson, James C.
CORPORATE SOURCE: School of Medicine, University of Miami, Miami, FL, 33176, USA
SOURCE: Annals of the New York Academy of Sciences (1997), 837(Preventive Strategies for Living in a Chemical World), 257-268
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The initial concns. of the **urinary** pesticide metabolites in poisoning were related to the chem. configuration of the pesticide, its metab. and toxicity , and the dose and route of metab. The **urinary** alkyl phosphates, while being highly sensitive indicators of organophosphate exposures, lacked specificity for individual organophosphate pesticides, making it impossible to uniformly predict **cholinesterase**-inhibition illness on the basis of a single **urinary** alkyl phosphate concn. after exposure to an unknown pesticide.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:749527 CAPLUS
DOCUMENT NUMBER: 128:44121
TITLE: M4 muscarinic autoreceptor-mediated inhibition of [3H]acetylcholine release in the rat isolated **urinary bladder**
AUTHOR(S): D'agostino, Gianluigi; Barbieri, Annalisa; Chiossa, Elena; Tonini, Marcello
CORPORATE SOURCE: Institute of Pharmacology, School of Pharmacy,

University of Pavia, Pavia, Italy
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1997), 283(2), 750-756
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A pharmacol. anal. was carried out in the rat **urinary bladder** to assess the nature of muscarinic receptors subtypes functionally involved in the neg. feedback mechanism regulating acetylcholine (ACh) secretion from postganglionic cholinergic nerve terminals and in smooth muscle contraction. **Bladder** strips were preincubated with 3H-choline, and the elec. evoked [3H]ACh release was detected simultaneously with contraction in the absence of **acetylcholinesterase** inhibitors. The effects were compared of seven muscarinic antagonists on [3H]ACh secretion (prejunctional effect) and muscle contraction (postjunctional effect). The rank order of postjunctional potencies (-log EC50) for the seven antagonists (atropine > 4-diphenylacetoxy-N-methylpiperidine methiodide (4-DAMP) > hexahydrosiladiphenidol hydrochloride (HHSiD) > tripitramine > pirenzepine > AF DX-116 > methoctramine) as well as their postjunctional affinity ests. (pA2) are in keeping with the notion that muscarinic receptors responsible for **bladder** contraction belong to the M3 subtype. The M3 subtype-preferring 4-DAMP and HHSiD did not discriminate between prejunctional and postjunctional effects. The M2/M4 subtype-preferring antagonists tripitramine, methoctramine and AF-DX 116 were more potent in facilitating the evoked [3H]ACh release than in inhibiting the contractile response. The rank order of prejunctional potencies was atropine > 4-DAMP > tripitramine > HHSiD > methoctramine > AF-DX 116 > pirenzepine, indicating the involvement of M4 receptors. Furthermore, when potency relationship was detd. by correlating prejunctional-log EC50 values with published consts. for cloned and natives muscarinic receptor subtypes, the correlations were significant for both M4 and M5 subtypes, but the best correlation found ($P < .001$) was for the M4 subtype. These findings suggest that the neg. feedback mechanism inhibiting the release of ACh in the rat **urinary bladder** is mediated by prejunctional autoreceptors of the M4 subtype.

L7 ANSWER 4 OF 328 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:539735 CAPLUS
DOCUMENT NUMBER: 127:231512

TITLE: Competitive enzyme immunoassay for **urinary** vanillylmandelic acid

AUTHOR(S): Taran, Frederic; Bernard, Herve; Valleix, Alain; Creminon, Christophe; Grassi, Jacques; Olichon, Didier; Deverre, Jean-Robert; Pradelles, Philippe
CORPORATE SOURCE: CEA, Service des Molecules Marquees DBCM, CEA-Saclay, Gif sur Yvette, 91191, Fr.

SOURCE: Clinica Chimica Acta (1997), 264(2), 177-192
CODEN: CCATAR; ISSN: 0009-8981
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An enzyme immunoassay for **urinary** vanillylmandelic acid (VMA) using polyclonal antiserum and VMA-**acetylcholinesterase** conjugate as enzymic tracer is described. Two different strategies for immunogen prepn. were developed and enantioselectivity was demonstrated. The selected EIA allowed direct measurement of **urinary** VMA using D(-)-VMA as std. with good sensitivity (MDC = 0.1 .mu.mol/L) and precision (CV <7% in 0.2-2.25 .mu.mol/L range). Cross-reactivity with homovanillic acid (HVA) was 0.8% and <0.4% with other structurally related catecholamine metabolites. Intra- and inter-assay repeatabilities were <10%, and recovery was 97.3% .+-. 3%. Good correlation was obtained for

EIA and HPLC anal. with normal and pathol. human urine samples (EIA = 0.895 HPLC-7.085, r2 = 0.98).

L7 ANSWER 5 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:460006 CAPLUS
DOCUMENT NUMBER: 127:103888
TITLE: Pharmacokinetics and safety of JTP-4819, a novel specific orally active prolyl endopeptidase inhibitor, in healthy male volunteers
AUTHOR(S): Umemura, K.; Kondo, K.; Ikeda, Y.; Kobayashi, T.; Urata, Y.; Nakashima, M.
CORPORATE SOURCE: Department of Pharmacology, Hamamatsu University School of Medicine, Hamamatsu, 431-31, Japan
SOURCE: British Journal of Clinical Pharmacology (1997), 43(6), 613-618
CODEN: BCPHBM; ISSN: 0306-5251
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In order to investigate the pharmacokinetics and safety profile of JTP-4819, (-)-(2S)-1-benzylaminocarbonyl-[(2S)-2-glycoloylpyrrolidinyl]-2-pyrrolidinecarboxamide, a novel specific orally active prolyl endopeptidase (PEP) inhibitor, JTP-4819 was given orally to 28 healthy male volunteers at single doses of 30 mg (n=6), 60 mg (n=6), 120 mg (n=6) and placebo (n=3) and multiple doses of 60 mg three times daily (n=5) and placebo (n=2) for 7 days to investigate its safety and pharmacokinetics following a preliminary safety evaluation of 3, 10 and 30 mg doses in six healthy volunteers. With the single dose of 60 mg, a cross-over study was conducted to examine the effect of food on the bioavailability of the drug. The concns. of JTP-4819 in plasma and urine were detd. by electrospray ionization-liq. chromatog./mass spectrometry (ESI-LC/MS) method. In the multiple-dose study, the **cholinesterase** activity was gradually increased and reached above the normal range on days 4 to 8 in all five subjects given JTP-4819 and gradually returned to normal range after completion of dosing. The elevation of plasma **cholinesterase** activity was considered to be an action of JTP-4819, but this remains to be verified. There were no other abnormal findings in objective symptoms and lab. findings including blood pressure, heart rate, ECG, body temp., hematol., blood chem. and urinalysis. The Cmax of JTP-4819 at 30, 60 and 120 mg in fasting state were 474, 887 and 1649 ng mL-1, resp., at 1 h after administration, and the t1/2 was about 2 h. AUC increased in proportion to the given doses. The cumulative **urinary** recoveries within 24 h were approx. 66%. Cmax, AUC, t1/2 and **urinary** recovery were not affected by food intake. In the multiple-dose study, there was no drug accumulation trend in plasma. These results indicate that JTP-4819 has acceptable pharmacodynamic and pharmacokinetics profiles for clin. use without any serious adverse events as we verified in healthy young male volunteers.

L7 ANSWER 6 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:437306 CAPLUS
DOCUMENT NUMBER: 127:91532
TITLE: Comparative evaluation on the biological monitoring of exposure to parathion and its methyl analog
AUTHOR(S): Chang, M. J. W.; Chen, Y. C.; Yang, H. J.
CORPORATE SOURCE: Toxicology/Pharmacology Laboratory, Chang Gung College of Medicine and Technology, Tao-Yuan, 333, Taiwan
SOURCE: Archives of Environmental Contamination and Toxicology (1997), 32(4), 422-425
CODEN: AECTCV; ISSN: 0090-4341
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of both parathion and methyl parathion on the inhibition of plasma **cholinesterase** were elaborated in a rat model employing a modified isocratic reversed-phase HPLC method coupled with UV detection for the detn. of the **urinary** metabolite p-nitrophenol (U-4NP). A linearity of r2 > 0.995 was found for a std. curve ranging from 0.06 to 0.96 .mu.g/mL with a % relative error of .ltoreq..+-.10% and a recovery of 89 .+-. 2%. The % CV at all levels was .ltoreq.11%. A linear correlation was obsd. between the oral administration of parathion and methyl parathion for both the percent inhibition of **cholinesterase** as well as the **urinary** elimination of 4NP. It is tentatively recommended that a U-4NP of 2.0 mg/g creatinine be established as a biol. exposure index (BEI) for methyl parathion.

L7 ANSWER 7 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:308490 CAPLUS
DOCUMENT NUMBER: 126:326662
TITLE: Biological monitoring of exposure to chloropyrifos-methyl by assay of **urinary** alkylphosphates and 3,5,6-trichloro-2-pyridinol
AUTHOR(S): Aprea, Cristina; Sciarra, Gianfranco; Sartorelli, Pietro; Sartorelli, Emilio; Strambi, Fabio; Farina, Giuseppe A.; Fattorini, Alessandro
CORPORATE SOURCE: Institute of Occupational Medicine, University of Siena, Siena, Italy
SOURCE: Journal of Toxicology and Environmental Health (1997), 50(6), 581-594
CODEN: JTEHD6; ISSN: 0098-4108
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The results of biol. monitoring by assay of **urinary** 3,5,6-trichloro-2-pyridinol and alkylphosphates (DMP, DMTP) in groups of 9 and 2 workers exposed to chlorpyrifos-Me during vine spraying and manual leaf thinning 5-11 d after spraying, resp., are reported. The results are compared with those of a control group of 46 subjects not occupationally exposed to organophosphate insecticides. Significantly higher **urinary** excretion of metabolites (Mann-Whitney U-test) was found in both groups than in controls. Levels of 3,5,6-trichloro-2-pyridinol (mean .+-. SD) were 15.9 .+-. 10.6 nmol/g creatinine (n = 33) for controls, 92.4 + 162.5 nmol/g creatinine (n = 20) for manual workers, and 675.5 + 1110.8 nmol/g creatinine (n = 48) for workers spraying and mixing the insecticide. Levels of DMP (mean .+-. SD) were 63.8 + 100.1 nmol/g creatinine (n = 42), 123.0 + 79.0 nmol/g creatinine (n = 20), and 577.2 + 1003.2 nmol/g creatinine (n = 61), resp., for the same 3 groups. Levels of DMTP (mean .+-. SD) were 153.4 + 164.4 nmol/g creatinine (n = 43), 489.3 + 288.3 nmol/g creatinine (n = 20), and 297.6 + 215.4 nmol/g creatinine (n = 61), resp., for the same 3 groups. Good correlations were found between **urinary** excretion of 3,5,6-trichloro-2-pyridinol and DMP (r = .776 for manual workers; r = .775 for workers mixing and spraying the insecticide) or DMTP (r = .558 and r = .746, resp. for the same 2 groups). The peak of excretion of the three metabolites was found in urine samples collected the night after the spraying or leaf thinning operations.

L7 ANSWER 8 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:101976 CAPLUS
DOCUMENT NUMBER: 126:209192
TITLE: Competitive enzyme immunoassay with monoclonal antibody for homovanillic acid measurement in human urine samples
AUTHOR(S): Taran, Frederic; Frobert, Yveline; Creminon, Christophe; Grassi, Jacques; Olichon, Didier; Mioskowski, Charles; Pradelles, Philippe

CORPORATE SOURCE: Service Molecules Marquees DBCM, CEA, Gif sur Yvette, 91191, Fr.
SOURCE: Clinical Chemistry (Washington, D. C.) (1997), 43(2), 363-368
CODEN: CLCHAU; ISSN: 0009-9147
PUBLISHER: American Association for Clinical Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A fast competitive enzyme immunoassay (EIA) for measuring homovanillic acid in human urine samples was developed with a monoclonal antibody and **acetylcholinesterase** as enzyme label. Enzyme detection was performed by an easy colorimetric assay. Monoclonal antibodies were screened on the basis of sensitivity, specificity, and correlation studies. EIA has a detection limit of 0.5 .mu.mol/L, a CV <10% in the 1.25-10 .mu.mol/L range, and intra- and interassay CVs of <10%. Cross-reactivity with vanillylmandelic acid was 0.5% and <8% for other structurally related catecholamine metabolites. Parallelism of the EIA was shown in diln. studies and the correlation with routine HPLC assay in 62 normal and pathol. samples was EIA = 1.492 (HPLC) - 3.46, Sy/x = 47.52, range = 4-1800 .mu.mol/L, r2 = 0.977. Addnl. data concerning the validity of this assay were provided by HPLC anal. of **urinary** immunoreactive material.

L7 ANSWER 9 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:99335 CAPLUS
DOCUMENT NUMBER: 126:134952
TITLE: Exposure of spraying workers in orchard to dichlorvos and the **urinary** excretion of its metabolites
AUTHOR(S): Okuno, Toshihiro; Yamamoto, Akio; Fujiwara, Tukimi; Fukase, Osamu
CORPORATE SOURCE: Div. Environ. Health, Hyogo Prefectural Inst. Public Health, Kobe, 652, Japan
SOURCE: Hyogo-kenritsu Eisei Kenkyusho Nenpo (1996), 31, 73-80
CODEN: HEKNFV; ISSN: 1342-6745
PUBLISHER: Hyogo-kenritsu Eisei Kenkyusho
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB To evaluate the level of exposure to organophosphorus insecticide dichlorvos (DDVP) to the spraying workers in an apple orchard, concns. of DDVP in the environment during spraying, **urinary** excretion of di-Me phosphate (DMP) (one of the metabolites of DDVP) and the blood examns. of 5 spraying workers and one observer were studied. The results obtained were as follows: (1) five workers sprayed 1.85 kg of DDVP and 3.7 kg of captan as active ingredient to the 248 are orchard for 5.5 h with an airblast sprayer. (2) DDVP and captan concns. in the air of the monitoring point were 1.0-15.4 .mu.g/m2 and 0.0 .mu.g/m3, resp. (3) DDVP and captan concns. near the worker's breathing zone were 113.6-765.3 .mu.g/m3 and 7.0-66.1 .mu.g/m3, resp. (4) DMP in urine was detected in all workers and observer. The levels were 64.2-417.2 .mu.g/day in the workers and 1.4 .mu.g/day in the observer. The max. concn. of DMP was obtained 12-16 h after the start of spraying. (5) In the workers the mean values of red cell count, Hb, hematocrit, serum total protein and serum **cholinesterase** activity were significantly decreased after spraying. Significant correlation was obsd. between levels of **urinary** excretion of DMP and the decrease serum ChE activity.

L7 ANSWER 10 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:44396 CAPLUS
DOCUMENT NUMBER: 126:43786
TITLE: Acephate Insecticide Toxicity: Safety Conferred by Inhibition of the Bioactivating Carboxyamidase by the Metabolite Methamidophos
AUTHOR(S): Mahajna, Mahmoud; Quistad, Gary B.; Casida, John E.

CORPORATE SOURCE: Environmental Chemistry and Toxicology Laboratory Department of Environmental Science Policy and Management, University of California, Berkeley, CA, 94720-3112, USA
SOURCE: Chemical Research in Toxicology (1997), 10(1), 64-69
CODEN: CRTOEC; ISSN: 0893-228X
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We show in the present investigation that a carboxyamidase activates acephate in mice and in turn undergoes inhibition by the hydrolysis product, i.e., methamidophos; thus, the bioactivation is started but immediately turned off. These relationships are established by finding that 4 h pretreatment of mice with methamidophos i.p. at 5 mg/kg has the following effects on acephate action: reduces methamidophos and acephate levels in liver by 30-60% in the first 2 h after i.p. acephate dosage; inhibits the liver carboxyamidase, cleaving [14CH3S]acephate to [14CH3S]methamidiphos with 50% block at .apprx.1 mg/kg; strongly inhibits 14CO2 liberation from [CH314C(O)]acephate in vivo; markedly alters the pattern of **urinary** metabolites of acephate by increasing O- and S-demethylation products retaining the carboxyamide moiety; greatly reduces the brain **acetylcholinesterase** (AChE) inhibition following acephate treatment; doubles the LD50 of i.p.-administered acephate from 540 to 1140 mg/kg. Methamidophos pretreatment in rats also markedly alters the metab. of dimethoate (another systemic insecticide) from principally carboxyamide hydrolysis to mainly other pathways. In contrast, methamidophos pretreatment of houseflies does not alter the acephate-induced toxicity and brain AChE inhibition. The safety of acephate in mammals therefore appears to be due to conversion in small part to methamidophos which, acting directly or as a metabolite, is a potent carboxyamidase inhibitor, thereby blocking further activation.

L7 ANSWER 11 OF 328 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:550753 CAPLUS
DOCUMENT NUMBER: 125:189065
TITLE: Automated measurement of **urinary cholinesterase** activity
AUTHOR(S): Matteucci, Elena; Giampietro, Ottavio
CORPORATE SOURCE: Istituto di Clinica Medica II, Universita di Pisa, Pisa, 56100, Italy
SOURCE: Laboratory Robotics and Automation (1996), 8(3), 161-163
CODEN: LRAUEY; ISSN: 0895-7533
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We propose the schedule of chem. parameters to program the assay of **urinary** cholinesterases (total, acetyl-, pseudo- and aliesterase) in a widely utilized automated analyzer (BM/Hitachi System 704 model). The program allows one to maximally simplify and abridge the assay procedure, yet it improves the quality of the enzymic reaction kinetics.

L7 ANSWER 12 OF 328 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:383042 CAPLUS
DOCUMENT NUMBER: 125:75250
TITLE: Identification of a 3-hydroxylated tacrine metabolite in rat and man: metabolic profiling implications and pharmacology
AUTHOR(S): Pool, William F.; Woolf, Thomas F.; Reily, Michael D.; Caprathe, Bradley W.; Emmerling, Mark R.; Jaen, Juan C.
CORPORATE SOURCE: Parke-Davis Pharmaceutical Research Div., Warner-Lambert Company, Ann Arbor, MI, 48105, USA

09/ 960,477

SOURCE: Journal of Medicinal Chemistry (1996), 39(15), 3014-3018
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Discrepancies in **urinary** metabolic profiles in rats administered tacrine suggested the presence of an unidentified metabolite of tacrine. Chromatog. methods were developed that allowed isolation of a metabolite fraction contg. both 1-hydroxytacrine and an unknown metabolite from rat urine. Mass spectral anal. indicated this metabolite to be a monohydroxylated deriv., which upon two dimensional COSY NMR anal. could be assigned as 3-hydroxytacrine. This structural assignment was confirmed by independent synthesis. 3-Hydroxytacrine was also identified as a human **urinary** metabolite of tacrine. Biol., this compd. was found to have in vitro human red blood cell **acetylcholinesterase** inhibitory activity similar to that of 1- and 4-hydroxytacrine and approx. 8-fold less than that of tacrine. These results underscore the need to conduct rigorous structural identification studies, esp. in cases where isomeric metabolites are possible, in assessing the accuracy of chromatog. profiling techniques.

L7 ANSWER 13 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:301927 CAPLUS
DOCUMENT NUMBER: 124:351180
TITLE: Exposure to sheep dip and the incidence of acute symptoms in a group of Welsh sheep farmers
AUTHOR(S): Rees, Huw
CORPORATE SOURCE: Health Department, University Hospital Wales, Cardiff, CF4 4XW, UK
SOURCE: Occupational and Environmental Medicine (1996), 53(4), 258-263
CODEN: OEMEEM; ISSN: 1351-0711
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The objective was to measure the exposure of a group of farmers to organophosphate pesticide in sheep dip, and to record the incidence of symptoms after exposure. A prospective study involved the autumn 1992 dipping period. Working methods were assessed by questionnaire. Absorption of organophosphate pesticide was estd. before, immediately after, and 6 wk after dipping by measuring plasma **cholinesterase**, erythrocyte **cholinesterase**, and dialkylphosphate **urinary** metabolites of organophosphates. Symptoms were recorded by questionnaire at the same time as biol. monitoring. Possible confounding factors were identified by medical examn. of the subjects. Three community council electoral wards in Powys, typical of hill sheep farming areas in Wales were used. All (38) men engaged in sheep dipping living in the 3 community council electoral wards. Twenty three sheep farmers and one dipping contractor completed the study, a response rate of 63%. A sample of 7 men who refused to enter the full study had similar working practices to the 24 subjects. Subjects reported inadequate handling precautions, and significant skin contamination with dip. Two men reported under dilg. dip conc. for use. Both had significant depression of erythrocyte **cholinesterase** after dipping. This indicated some absorption of organophosphate pesticide, but this did not reach levels usually assocd. with toxicity. It was not clear whether the symptoms of these 2 men were caused by organophosphate exposure. Measurement of dialkylphosphate **urinary** metabolites in a single specimen of urine voided shortly after the end of dipping could not be correlated with individual exposure. Sheep dipping is strenuous and dirty work and sheep farmers find it difficult to wear personal protective equipment and avoid skin contamination with dip. In this limited study,

farmers did not seem to have significant organophosphate toxicity, despite using inadequate handling precautions.

L7 ANSWER 14 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:83624 CAPLUS
DOCUMENT NUMBER: 124:126719
TITLE: Effects of exposure to lead on selected biochemical and hematological variables
AUTHOR(S): Solliway, Bernard M.; Schaffer, Alex; Pratt, Hillel; Yannai, Shamuel
CORPORATE SOURCE: Dep. Food Eng. Biotechnol., Herzliya Med. Center, Israel
SOURCE: Pharmacology & Toxicology (Copenhagen) (1996), 78(1), 18-22
CODEN: PHTOEH; ISSN: 0901-9928
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Blood and urine samples were taken form 34 persons occupationally exposed to lead and from 56 non-exposed control persons and blood lead and Hb concns., red blood cell count, erythrocyte glutathione peroxidase (GSH-peroxidase) and **acetylcholinesterase** (AChE), and **urinary** .delta.-aminolevulinic acid were detd. Blood lead concns. of the lead-exposed subjects were within the range generally accepted as safe for occupational-exposed adults in many countries (i.e. below 50 .mu.g Pb/dL blood). Yet, significant dose-dependent elevations were found in erythrocyte GSH-peroxidase and **urinary** .delta.-aminolevulinic acid. The **urinary** .delta.-aminolevulinic acid concn. of lead-exposed smokers was significantly elevated over that of lead-exposed non-smokers. Smoking did not affect the **urinary** .delta.-aminoleulinic acid concn. of control persons. In addn., a statistically significantly lower red blood cell count was obsd. in the lead-exposed group. Our results indicate that the above described safety std. for blood lead concns. in occupationally expose adults, although generally accepted, needs revision.

L7 ANSWER 15 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:82370 CAPLUS
DOCUMENT NUMBER: 124:138255
TITLE: Coumaphos intoxications mimic food poisoning
AUTHOR(S): Fang, Te-Chao; Chen, Kuan-Wen; Wu, Ming-Ho; Sung, Junne-Ming; Huang, Jeng-Jong
CORPORATE SOURCE: Department of Emergency Medicine, National Cheng Kung University Hospital, Tainan, 70428, Taiwan
SOURCE: Journal of Toxicology, Clinical Toxicology (1995), 33(6), 699-703
CODEN: JTCTDW; ISSN: 0731-3810
PUBLISHER: Dekker
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Reports of food poisoning caused by pesticide-contaminated food are rare in the medical literature. In this paper, we report six patients who suffered food poisoning in two sep. episodes in which the pesticide coumaphos was apparently misused as a food flavoring. These six patients presented not only the general manifestations of gastroenteritis, but also some unusual extra-intestinal symptoms. These included cholinergic overactivity (miosis, **urinary incontinence** and hypersalivation) that led us to suspect organophosphate intoxication. This diagnosis was confirmed by serial changes in RBC **cholinesterase** and pseudocholinesterase activity, and by the presence of coumaphos in the contaminated food. Of the six patients, one was dead on arrival. Another patient developed progressive respiratory failure and required mech. ventilation. The mortality rate among our

cases was 16.7%. Since the coumaphos was apparently added to food during cooking, its toxic effects do not appear to be mitigated by heating. When food poisoning cases present with both gastroenteritis and unusual autonomic symptoms, the autonomic syndromes will aid in the diagnosis and management of these critically ill patients.

L7 ANSWER 16 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:26365 CAPLUS
DOCUMENT NUMBER: 124:78775
TITLE: A review of nonpesticide phosphate ester-induced neurotoxicity in cattle
AUTHOR(S): Coppock, R W.; Mostrom, M S.; Khan, A A.; Stair, E L.
CORPORATE SOURCE: Alberta Environmental Centre, Vegreville, AB, T9C 1T4, Can.
SOURCE: Veterinary and Human Toxicology (1995), 37(6), 576-9
CODEN: VHTODE; ISSN: 0145-6296
PUBLISHER: American Academy of Veterinary and Comparative Toxicology
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion with 20 refs. Nonpesticide phosphate esters induce delayed neurotoxicity in cattle. The most common exposures are to complex mixts. of triaryl phosphates used in lubricating oils. Oral ingestion is most common, but dermal exposures have also occurred. Clin. signs of **cholinesterase** (ChE) inhibition may or may not be seen. Depending on the biochem. targets, the percent redn. in blood ChE is variable and can be <30% of normal activity. Organophosphate ester-induced delayed neurotoxicity cannot be predicted by inhibition of blood ChEs. Signs of delayed neurotoxicity occur 2 to 25 d after exposure; these signs are neurol. deficiencies of the antigravity muscles and the muscles of the **urinary bladder** and larynx.
Affected cattle may dribble urine and some may be mute. Signs of ChE inhibition generally are not obsd. in animals with neurol. deficiencies. Pathol. findings are axonopathy and myelin degeneration of nerves with long axons located in both the peripheral and central nervous systems. In the spinal cord, location of the affected nerve tracts is variable. Degenerative changes occur in motor neurons. Calves are less susceptible to organophosphate ester-induced delayed neurotoxicity than cows. A dose of 500 mg triaryl phosphate/kg will produce complete paralysis in a mature cow in 26 d.

L7 ANSWER 17 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:909944 CAPLUS
DOCUMENT NUMBER: 124:27374
TITLE: Leukocytosis as a marker of organ damage induced by chronic strenuous physical exercise
AUTHOR(S): Kayashima, S.; Ohno, H.; Fujioka, T.; Taniguchi, N.; Nagata, N.
CORPORATE SOURCE: Third Department of Internal Medicine, National Defense Medical College, Tokorozawa, 359, Japan
SOURCE: European Journal of Applied Physiology and Occupational Physiology (1995), 70(5), 413-20
CODEN: EJAPCK; ISSN: 0301-5548
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of strenuous phys. exercise on the serial changes in hematol., biochem. and hormonal markers were investigated. A group of 14 soldiers, aged 24-36 yr, took part in a military training course for about 13 wk. After severe exercise stress, an increase (90%) in the no. of peripheral blood leukocytes was obsd. The degree of leukocytosis showed a close correlation with the values of some serum parameters, such as concns. of aspartate aminotransferase (AST; r = 0.747), lactate dehydrogenase (LD; r

= 0.748), blood urea nitrogen (r = 0.756), creatine kinase (CK; r = 0.637), manganese-superoxide dismutase (Mn-SOD; r = 0.508), alanine aminotransferase (ALT; r = 0.542) and uric acid (r = 0.538), and concns. of **urinary** parameters, such as vanilmandelic acid (r = 0.429) and free cortisol (r = 0.437). The subjects showing prominent leukocytosis over 9500 cells .cntdot. .mu.L-1 exhibited a lower concn. of serum **cholinesterase** than those who showed milder leukocytosis. The serum Mn-SOD concn. was closely correlated with the serial changes in serum concns. of AST, ALT, LD and CK, indicating exercise-induced muscle and liver damage. The change in peripheral leukocyte no. was assumed to be diagnostically informative and may be a prognostic marker, reflecting organ damage and restoration after strenuous phys. exercise.

L7 ANSWER 18 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:754816 CAPLUS
DOCUMENT NUMBER: 123:178173
TITLE: Assessment of omethoate and fenitrothion absorption in greenhouse workers using personal protection equipment in confined areas
AUTHOR(S): Aprea, C.; Sciarra, G.; Sartorelli, P.; Ceccarelli, F.; Maiorano, M.; Savelli, G.
CORPORATE SOURCE: Ist. Med. Lavoro, Univ. Studi Siena, Siena, 53100, Italy
SOURCE: Medicina del Lavoro (1994), 85(3), 242-8
CODEN: MELAAD; ISSN: 0025-7818
PUBLISHER: Medicina del Lavoro
DOCUMENT TYPE: Journal
LANGUAGE: Italian
AB Sprayers and workers engaged in manual operations in a greenhouse were monitored for exposure to omethoate and fenitrothion. **Urinary** dialkylphosphates (dimethylthiophosphate and dimethylphosphate) were used as a biol. index of exposure to the two chems. Residues of fenitrothion on foliage were measured as well as levels of fenitrothion and omethoate in air samples collected in the breathing zone (personal sampling) and in the work-place near the entrance and the end of the greenhouse (static sampling). Skin exposure was estd. from pads placed on the thorax under overalls and from hand washing liq. at the end of the workshift. Sprayers wore respiratory and skin protection during the workshift. Workers engaged in manual operations did not wear respiratory protection. Re-entry to the greenhouse was permitted 48 h after spraying. Levels of omethoate and fenitrothion in air samples, on pads and on the hands, during manual operations on ornamental plants, were low. Urine anal. shoved no significant difference between the pre- and post-exposure samples. No significant difference was found between levels of **urinary** dialkylphosphates in the control group and exposed workers. **Cholinesterase** activity (acetyl and butyryl) showed no significant redn. at the end of the workshift compared with baseline values.

L7 ANSWER 19 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:697617 CAPLUS
DOCUMENT NUMBER: 123:101985
TITLE: The **acetylcholinesterase** oxime reactivator HI-6 in man: pharmacokinetics and tolerability in combination with atropine
AUTHOR(S): Clement, John G.; Bailey, David G.; Madill, Herbert D.; Tran, Lan T.; Spence, J. David
CORPORATE SOURCE: Defence Res. Establishment Suffield, Ralston, AB, Can.
SOURCE: Biopharmaceutics & Drug Disposition (1995), 16(5), 415-25
CODEN: BDDID8; ISSN: 0142-2782
PUBLISHER: Wiley
DOCUMENT TYPE: Journal

LANGUAGE: English

AB In a double-blind, placebo-controlled, single-dose ascending pharmacokinetics and tolerance study, we evaluated the bispyridinium oxime HI-6 dichloride monohydrate (62.5, 125, 250, and 500 mg), administered i.m. with atropine sulfate, 2 mg, in 24 healthy male volunteers. The plasma HI-6 peak concn. (Cmax) and area under the concn.-time curve (AUC) demonstrated linear pharmacokinetics with low intradose variability, suggestive of uniformity of effect among subjects. HI-6 (500 mg) attained plasma drug concns. that appeared adequate for practical use as an antidote. The mean .+-. SD time to max. plasma HI-6 concn. (tmax = 0.69 .+-. 0.21 h, n = 16), and absorption half-life (t/2a = 0.17 .+-. 0.05 h) indicated rapid onset of effect. The vol. of distribution (Vd = 0.25 .+-. 0.04 L kg-1 TBW) approximated the extracellular fluid vol. A high total body clearance (CL = 252 .+-. 52 mL min-1) and short apparent elimination half-life (t/2e = 1.15 .+-. 0.19 h) were expected for this polar quaternary ammonium drug. The renal clearance (CLr = 137 .+-. 33 mL min-1), which approximated the expected glomerular filtration rate, and 24 h **urinary** excretion of unchanged drug (55 .+-. 10%) indicated substantial non-renal elimination. Blood pressure, heart rate, respiratory rate, electrocardiog. parameters, mental acuity, and vision were not altered. Adverse events and changes in serum, urine, and semen lab. tests were mild. The pharmacokinetics, safety, and apparent efficacy of HI-6 suggest it may be a superior oxime antidote against nerve agent poisoning.

L7 ANSWER 20 OF 328 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:639481 CAPLUS
DOCUMENT NUMBER: 123:39952
TITLE: Use of **urinary** p-nitrophenol as an index of exposure to parathion
AUTHOR(S): Denga, N.; Moldeus, P.; Kasilo, O. M. J.; Nhachi, C. F. B.
CORPORATE SOURCE: Dep. Clin. Pharm., Univ. Zimbabwe, Harare, Zimbabwe
SOURCE: Bulletin of Environmental Contamination and Toxicology (1995), 55(2), 296-302
CODEN: BECTA6; ISSN: 0007-4861
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To establish the use of **urinary** p-nitrophenol as a bio-marker of parathion exposure in humans, male rabbits were injected with parathion to compare their **urinary** p-nitrophenol levels with anti-**cholinesterase** activity of parathion in blood. In 2 methods used to assay **urinary** p-nitrophenol, p-nitrophenol was not detectable in control animals; however, **urinary** p-nitrophenol was detected 24 h after parathion administration and peaked after 48 h. The Moldeus method was used as an index of parathion exposure in humans. A total of 21 coffee parathion sprayers were evaluated for possible exposure to parathion. Results showed that **urinary** p-nitrophenol may be used as a human bio-marker for parathion exposure, but not necessarily for the extent of exposure.

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(FILE 'HOME' ENTERED AT 17:48:50 ON 27 JUN 2003)

FILE 'CAPLUS' ENTERED AT 17:49:18 ON 27 JUN 2003
L1 387 S (ACETYLCHOLINESTERASE OR CHOLINESTERASE) AND (URINARY OR BLAD
L2 2 S L1 AND PYRROLO
L3 385 S L1 NOT L2
L4 345 S L3 NOT PY>1998
L5 1 S L4 AND (TRICYCLIC OR TRICYCLE?)

09/ 960,477

L6 344 S L4 NOT L5
L7 328 S L6 NOT PY>1997

=> s l7 and inhibitor?
832454 INHIBITOR?
L8 39 L7 AND INHIBITOR?

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YOU HAVE REQUESTED DATA FROM 39 ANSWERS - CONTINUE? Y/(N):y

L8 ANSWER 1 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:749527 CAPLUS
DOCUMENT NUMBER: 128:44121
TITLE: M4 muscarinic autoreceptor-mediated inhibition of [3H]acetylcholine release in the rat isolated **urinary bladder**
AUTHOR(S): D'agostino, Gianluigi; Barbieri, Annalisa; Chiossa, Elena; Tonini, Marcello
CORPORATE SOURCE: Institute of Pharmacology, School of Pharmacy, University of Pavia, Pavia, Italy
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1997), 283(2), 750-756
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A pharmacol. anal. was carried out in the rat **urinary bladder** to assess the nature of muscarinic receptors subtypes functionally involved in the neg. feedback mechanism regulating acetylcholine (ACh) secretion from postganglionic cholinergic nerve terminals and in smooth muscle contraction. **Bladder** strips were preincubated with 3H-choline, and the elec. evoked [3H]ACh release was detected simultaneously with contraction in the absence of **acetylcholinesterase inhibitors**. The effects were compared of seven muscarinic antagonists on [3H]ACh secretion (prejunctional effect) and muscle contraction (postjunctional effect). The rank order of postjunctional potencies (-log EC50) for the seven antagonists (atropine > 4-diphenylacetoxy-N-methylpiperidine methiodide (4-DAMP) > hexahydrosiladiphenidol hydrochloride (HHSiD) > tripitramine > pirenzepine > AF DX-116 > methoctramine) as well as their postjunctional affinity ests. (pA2) are in keeping with the notion that muscarinic receptors responsible for **bladder** contraction belong to the M3 subtype. The M3 subtype-preferring 4-DAMP and HHSiD did not discriminate between prejunctional and postjunctional effects. The M2/M4 subtype-preferring antagonists tripitramine, methoctramine and AF-DX 116 were more potent in facilitating the evoked [3H]ACh release than in inhibiting the contractile response. The rank order of prejunctional potencies was atropine > 4-DAMP > tripitramine > HHSiD > methoctramine > AF-DX 116 > pirenzepine, indicating the involvement of M4 receptors. Furthermore, when potency relationship was detd. by correlating prejunctional-log EC50 values with published consts. for cloned and natives muscarinic receptor subtypes, the correlations were significant for both M4 and M5 subtypes, but the best correlation found ($P < .001$) was for the M4 subtype. These findings suggest that the neg. feedback mechanism inhibiting the release of ACh in the rat **urinary bladder** is mediated by prejunctional autoreceptors of the M4 subtype.

L8 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:460006 CAPLUS
DOCUMENT NUMBER: 127:103888
TITLE: Pharmacokinetics and safety of JTP-4819, a novel specific orally active prolyl endopeptidase

inhibitor, in healthy male volunteers

AUTHOR(S): Umemura, K.; Kondo, K.; Ikeda, Y.; Kobayashi, T.; Urata, Y.; Nakashima, M.
CORPORATE SOURCE: Department of Pharmacology, Hamamatsu University School of Medicine, Hamamatsu, 431-31, Japan
SOURCE: British Journal of Clinical Pharmacology (1997), 43(6), 613-618
CODEN: BCPHBM; ISSN: 0306-5251
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In order to investigate the pharmacokinetics and safety profile of JTP-4819, (-)-(2S)-1-benzylaminocarbonyl-[(2S)-2-glycoloylpyrrolidinyl]-2-pyrrolidinecarboxamide, a novel specific orally active prolyl endopeptidase (PEP) **inhibitor**, JTP-4819 was given orally to 28 healthy male volunteers at single doses of 30 mg (n=6), 60 mg (n=6), 120 mg (n=6) and placebo (n=3) and multiple doses of 60 mg three times daily (n=5) and placebo (n=2) for 7 days to investigate its safety and pharmacokinetics following a preliminary safety evaluation of 3, 10 and 30 mg doses in six healthy volunteers. With the single dose of 60 mg, a cross-over study was conducted to examine the effect of food on the bioavailability of the drug. The concns. of JTP-4819 in plasma and urine were detd. by electrospray ionization-liq. chromatog./mass spectrometry (ESI-LC/MS) method. In the multiple-dose study, the **cholinesterase** activity was gradually increased and reached above the normal range on days 4 to 8 in all five subjects given JTP-4819 and gradually returned to normal range after completion of dosing. The elevation of plasma **cholinesterase** activity was considered to be an action of JTP-4819, but this remains to be verified. There were no other abnormal findings in objective symptoms and lab. findings including blood pressure, heart rate, ECG, body temp., hematol., blood chem. and urinalysis. The Cmax of JTP-4819 at 30, 60 and 120 mg in fasting state were 474, 887 and 1649 ng mL-1, resp., at 1 h after administration, and the t1/2 was about 2 h. AUC increased in proportion to the given doses. The cumulative **urinary** recoveries within 24 h were approx. 66%. Cmax, AUC, t1/2 and **urinary** recovery were not affected by food intake. In the multiple-dose study, there was no drug accumulation trend in plasma. These results indicate that JTP-4819 has acceptable pharmacodynamic and pharmacokinetics profiles for clin. use without any serious adverse events as we verified in healthy young male volunteers.

L8 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:44396 CAPLUS
DOCUMENT NUMBER: 126:43786
TITLE: Acephate Insecticide Toxicity: Safety Conferred by Inhibition of the Bioactivating Carboxyamidase by the Metabolite Methamidophos
AUTHOR(S): Mahajna, Mahmoud; Quistad, Gary B.; Casida, John E.
CORPORATE SOURCE: Environmental Chemistry and Toxicology Laboratory Department of Environmental Science Policy and Management, University of California, Berkeley, CA, 94720-3112, USA
SOURCE: Chemical Research in Toxicology (1997), 10(1), 64-69
CODEN: CRTOEC; ISSN: 0893-228X
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We show in the present investigation that a carboxyamidase activates acephate in mice and in turn undergoes inhibition by the hydrolysis product, i.e., methamidophos; thus, the bioactivation is started but immediately turned off. These relationships are established by finding that 4 h pretreatment of mice with methamidophos i.p. at 5 mg/kg has the following effects on acephate action: reduces methamidophos and acephate

levels in liver by 30-60% in the first 2 h after i.p. acephate dosage; inhibits the liver carboxyamidase, cleaving [14CH3S]acephate to [14CH3S]methamidiphos with 50% block at .apprx.1 mg/kg; strongly inhibits 14CO2 liberation from [CH314C(O)]acephate in vivo; markedly alters the pattern of **urinary** metabolites of acephate by increasing O- and S-demethylation products retaining the carboxyamide moiety; greatly reduces the brain **acetylcholinesterase** (AChE) inhibition following acephate treatment; doubles the LD50 of i.p.-administered acephate from 540 to 1140 mg/kg. Methamidophos pretreatment in rats also markedly alters the metab. of dimethoate (another systemic insecticide) from principally carboxyamide hydrolysis to mainly other pathways. In contrast, methamidophos pretreatment of houseflies does not alter the acephate-induced toxicity and brain AChE inhibition. The safety of acephate in mammals therefore appears to be due to conversion in small part to methamidophos which, acting directly or as a metabolite, is a potent carboxyamidase **inhibitor**, thereby blocking further activation.

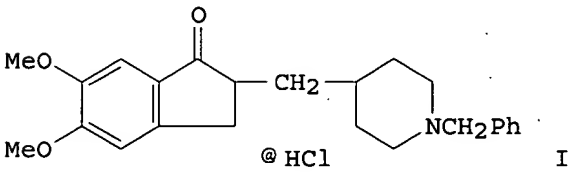
L8 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:383042 CAPLUS
DOCUMENT NUMBER: 125:75250
TITLE: Identification of a 3-hydroxylated tacrine metabolite in rat and man: metabolic profiling implications and pharmacology
AUTHOR(S): Pool, William F.; Woolf, Thomas F.; Reily, Michael D.; Caprathe, Bradley W.; Emmerling, Mark R.; Jaen, Juan C.
CORPORATE SOURCE: Parke-Davis Pharmaceutical Research Div., Warner-Lambert Company, Ann Arbor, MI, 48105, USA
SOURCE: Journal of Medicinal Chemistry (1996), 39(15), 3014-3018
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Discrepancies in **urinary** metabolic profiles in rats administered tacrine suggested the presence of an unidentified metabolite of tacrine. Chromatog. methods were developed that allowed isolation of a metabolite fraction contg. both 1-hydroxytacrine and an unknown metabolite from rat urine. Mass spectral anal. indicated this metabolite to be a monohydroxylated deriv., which upon two dimensional COSY NMR anal. could be assigned as 3-hydroxytacrine. This structural assignment was confirmed by independent synthesis. 3-Hydroxytacrine was also identified as a human **urinary** metabolite of tacrine. Biol., this compd. was found to have in vitro human red blood cell **acetylcholinesterase** **inhibitory** activity similar to that of 1- and 4-hydroxytacrine and approx. 8-fold less than that of tacrine. These results underscore the need to conduct rigorous structural identification studies, esp. in cases where isomeric metabolites are possible, in assessing the accuracy of chromatog. profiling techniques.

L8 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:695745 CAPLUS
DOCUMENT NUMBER: 121:295745
TITLE: **Urinary cholinesterase** in normal people: A reappraisal
AUTHOR(S): Matteucci, E.; Pellegrini, L.; Cecere, M.; Uncini-Manganelli, C.; Giampietro, O.
CORPORATE SOURCE: Ist. di Clin. Med. II, Univ. degli Stud., Pisa, Italy
SOURCE: European Journal of Laboratory Medicine (1993), 1(1), 13-17
CODEN: EJLAEW; ISSN: 1122-8652
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Esterase, a heterogeneous group of enzymes catalyzing hydrolysis of ester bands, has multiple **inhibitor** and substrate specificities. **Cholinesterase**, which hydrolyzes choline ester at a higher rate, has been localized in mammalian kidneys. But data in the literature on its appearance in urine are contradictory. Esterase activity has been measured on the second urine sample in the morning from 27 healthy subjects by using acetylthiocholine as substrate and two different **inhibitors**: eserine to inactivate both **acetylcholinesterase** and pseudocholinesterase, and quinidine to inactivate pseudocholinesterase only. Total esterase activity (4.86 U/L, centrifuged specimens) has been divided into eserine-resistant esterases (aliesterases, 2.67 U/L) and eserine-sensitive esterases (cholinesterases, 2.31 U/L). The procedure described allowed the authors to obtain good quality enzyme kinetics and reproducible results: sample centrifugation before assay was found unnecessary, while immediate assays seem crucial in the measurement of intact enzymic activities.

L8 ANSWER 6 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:573528 CAPLUS
DOCUMENT NUMBER: 119:173528
TITLE: Pharmacokinetics of E2020, a new compound for Alzheimer's disease, in healthy male volunteers
AUTHOR(S): Mihara, M.; Ohnishi, A.; Tomono, Y.; Hasegawa, J.; Shimamura, Y.; Yamazaki, K.; Morishita, N.
CORPORATE SOURCE: Res. Dev. Div., Eisai Co., Ltd., Tokyo, 112-88, Japan
SOURCE: International Journal of Clinical Pharmacology, Therapy and Toxicology (1993), 31(5), 223-9
CODEN: IJCPB5; ISSN: 0300-9718
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB E2020 (I) is a new **cholinesterase inhibitor** with a novel chem. structure, which is under clin. investigation for use in Alzheimer's disease in Japan and the USA. Three sep. studies were conducted to evaluate the safety and to establish the pharmacokinetic profile of E2020 after oral administration to healthy male subjects. E2020 was administered as: (1) single oral doses (0.3 mg, 1 mg, 2 mg, 5 mg, 8 mg and 10 mg) in a fasting condition, (2) a single oral dose (2 mg) after a meal and (3) repeated oral doses (2 mg once daily for 21 days). The concns. of E2020 and its metabolites in plasma, serum, urine and feces were detd. by HPLC methods with UV detection. E2020 was generally well tolerated by all subjects. In the single-dose study, there was a linear relationship between dose and mean AUC. The mean plasma half-life was about 50 h and was dose-independent. The total clearance and renal clearance of E2020 were also dose-independent and the mean values after 10 mg dosing were 9.7 L/h and 0.86 L/h, resp. The cumulative total **urinary** and fecal excretion of the sum of unchanged E2020 and its metabolites at 264 h after the administration of the single 10 mg dose was 36.1% and 8.6% of the dose, resp. The mean serum protein binding was 92.6%. No effect of food intake on the pharmacokinetics was obsd. Evaluation of the mean trough levels and AUC0-24 of E2020 indicated that a

steady-state was achieved after approx. 2 wk of daily dosing.

L8 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:232422 CAPLUS
DOCUMENT NUMBER: 116:232422
TITLE: **Acetylcholinesterase** and ADH-stimulated water permeability in the amphibian **urinary bladder**
AUTHOR(S): Bagrov, Ya. Yu.; Manusova, N. B.; Ostretsova, I. B.
CORPORATE SOURCE: Inst. Evol. Physiol. Biochem., St. Petersburg, Russia
SOURCE: Tsitologiya (1991), 33(11), 141-52
CODEN: TSITAQ; ISSN: 0041-3771
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Acetylcholine (ACh) at the concn. of 10-3M inhibited ADH-stimulated water transport through the wall of amphibian **urinary bladder**. This effect was suggested to be caused by an interaction of ACh with **acetylcholinesterase** (AChE) rather than by a stimulation of the M- or N-cholinoreceptor. The **inhibitory** action of ACh was completely suppressed in the presence of various AChE **inhibitors** (physostigmine, proserine, armine, Gd-42, acridine-iodomethylate), while an **inhibitor** of butyrylcholinesterase (BuChE), AD-4, failed to affect it. In accord with this observation the activity of AChE (but not of BuChE) was demonstrated in the **urinary bladder** epithelium. Since, in addn. to the hydroosmotic effects of pituitrin, 8-arginine-vasopressin, or oxytocin, ACh blocked also effects of forskolin or cAMP, one may conclude that it acts at some post-cAMP prodn. stage. AChE-dependent inhibition of the ADH-stimulated water transport decreased when the serosal pH was raising from 7.2 to 8.0, but was augmented by serosal acidification (pH 6.8), whereas such pH alterations did not affect the activity of the epithelium AChE. The effect of ACh under consideration was suppressed by adding amiloride (10-4M) to the serosal soln. Similarly, the ACh effect was blocked by an **inhibitor** of Ca-dependent K+ channels, 4-aminopyridine, which in addn. prevented the inhibition of the ADH-stimulated water transport by the serosal acidification. It was noteworthy that some other K+ channel blockers (Ba2+, Cs+, tetraethylammonium, apamine, quinine) did not affect either the water transport or the antipituitrin effect of ACh. Apparently, the **inhibitory** action of ACh on the ADH-stimulated water transport in the **urinary bladder** is mediated through the intracellular acidification resulting from ACh interaction with AChE. It is unlikely that the acidification is merely a consequence of the ACh hydrolysis, rather the ACh-AChE interaction induces directly an increase in the proton cond. of the basolateral membrane of the **urinary bladder** epithelium.

L8 ANSWER 8 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:401531 CAPLUS
DOCUMENT NUMBER: 115:1531
TITLE: Facilitatory effects of tachykinins and guanethidine on the acetylcholine output stimulated by nicotine from guinea pig **bladder**
AUTHOR(S): Shinkai, Michiko; Takayanagi, Issei; Kato, Teruko
CORPORATE SOURCE: Sch. Pharm. Sci., Toho Univ., Funabashi, Japan
SOURCE: British Journal of Pharmacology (1991), 103(1), 1191-5
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Contractile responses and acetylcholine release evoked by nicotine in guinea pig detrusor strips were detd. by isotonic transducer and RIA, resp. Nicotine stimulated acetylcholine release and a contractile response in guinea pig detrusor strips treated with the **cholinesterase inhibitor**, methanesulfonyl fluoride

(MSF). Both actions actions evoked by nicotine were antagonized by the nicotinic receptor antagonist hexamethonium but were insensitive to tetrodotoxin. A sympathetic nerve blocker, guanethidine and a tachykinin antagonist, [D-Arg2, D-Pro2, D-Trp7,9, Leu11]-substance P (rpwwL-SP) partially inhibited the acetylcholine release evoked by nicotine to much the same degree. The **inhibitory** effects of guanethidine and rpwwL-SP on acetylcholine release were greater than corresponding effects on the contraction evoked by nicotine. In prepns. treated with rpwwL-SP to block the tachykinin receptors, guanethidine had no effect on the response to nicotine. Conversely, after treatment with guanethidine to block release of a mediator from sympathetic nerve endings, nicotine-induced responses were not affected by rpwwL-SP. Nicotine-induced contraction was reduced to 30% by the muscarinic cholinoceptor antagonist atropine and was completely abolished after desensitization of P2-purinoceptors with .alpha.,.beta.-methylene ATP in the presence of atropine. A concn.-contractile response curve to neurokinin A (NKA) was shifted to the left after **cholinesterase** inhibition with MSF. Atropine abolished the facilitatory effect of MSF and partially inhibited contractions induced by NKA at 100 nM to 1 .mu.M. The contractile responses to substance P Me ester (SPOMe) and Tyr0-neurokinin B were not influenced by MSF or atropine. After desensitization of NK1 tachykinin receptors with SPOMe or preincubation with senktide, the cholinergic component of the nicotine-induced contraction was the same as the control value (100%). These findings give further support to previous results: nicotine stimulates acetylcholine release in a tetrodotoxin-resistant manner in guinea pig **bladder** and acetylcholine release evoked by nicotine is increased by the coordinated action of sympathetic nerves and tachykinin(s). It is suggested that the tachykinin receptor subtype involved in acetylcholine release is NK.

L8 ANSWER 9 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:201262 CAPLUS
DOCUMENT NUMBER: 114:201262
TITLE: Direct and indirect effects of **cholinesterase inhibitors** at muscarinic, adrenergic, and purinergic sites in parasympathetic ganglia
AUTHOR(S): Shinnick-Galligher, P.
CORPORATE SOURCE: Dep. Pharmacol. Toxicol., Univ. Texas, Galveston, TX, USA
SOURCE: Report (1989), Order No. AD-A220538, 28 pp. Avail.: NTIS
From: Gov. Rep. Announce. Index (U. S.) 1990, 90(16), Abstr. No. 041,113
DOCUMENT TYPE: Report
LANGUAGE: English
AB These studies analyzed, using intracellular recording methodol., the direct and indirect actions of soman and the effects of pyridostigmine at muscarinic **inhibitory** sites and on active and passive properties of neuronal membranes in cat **bladder** parasympathetic ganglia. The effect of pretreatment with pyridostigmine on soman was also analyzed. Low concns. of pyridostigmine enhanced submaximal muscarinic slow **inhibitory** postsynaptic potentials and responses to exogenously applied acetylcholine. In contrast, large amplitude s-ipsps, and ACh hyperpolarizations were depressed. The duration of the responses were prolonged in a concn.-dependent manner. Soman depressed the amplitude and prolonged the duration of a s-ipsp and ACh-induced hyperpolarization in a dose-dependent manner. Effects on amplitude were partially reversible; those on duration were irreversible. Soman enhanced nicotinic fast-epsps at the same time that s-ipsps were blocked. The **inhibitory** action of soman on the s-ipsp was prevented by pyridostigmine but not by atropine. A second application of soman did not further augment the effect of a first application. Both pyridostigmine and soman hyperbolized

the membrane and decreased input resistance in a reversible manner; soman effect could be recorded in the presence of atropine. Pyridostigmine and soman also reduced the half-maximal duration of the AHP following a directly elicited action potential. These results suggest that soman and pyridostigmine affect the muscarinic hyperpolarization through a postsynaptic action probably through AChE inhibition.

L8 ANSWER 10 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:76910 CAPLUS
DOCUMENT NUMBER: 114:76910
TITLE: Composition of technical ethephon [(2-chloroethyl)phosphonic acid] and some analogs relative to their reactivity and biological activity
AUTHOR(S): Segall, Yoffi; Grendell, Richard L.; Toia, Robert F.; Casida, John E.
CORPORATE SOURCE: Dep. Entomol. Sci., Univ. California, Berkeley, CA, 94720, USA
SOURCE: Journal of Agricultural and Food Chemistry (1991), 39(2), 380-5
CODEN: JAFCAU; ISSN: 0021-8561
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:76910
AB The phosphorus-contg. components in tech. ethephon, ClCH2CH2P(O)(OH)2, were assigned by comparisons with stds. from synthesis involving 31P NMR and GC/CI-MS (after derivatization with diazomethane). They were ClCH2CH2P(O)(OH)2 (90%), (HO)2P(O)CH2CH2P(O)(OH)2 (3%), ClCH2CH2P(O)(OH)OCH2CH2Cl, ClCH2CH2OCH2CH2P(O)(OH)2, and H2C:CHP(O)(OH)2 (each 1.5-1.8%), and HOCH2CH2P(O)(OH)2, HP(O)(OH)2, and HOP(O)(OH)2 (each 0.3-0.6%), consistent with the synthetic route starting with tris(2-chloroethyl) phosphite and involving Arbuzov rearrangement and various hydrolysis and dehydrochlorination reactions. **Urinary** products of tech. ethephon in rats are the parent compd., HOP(O)(OH)2, and unmetabolized (HO)2P(O)CH2CH2P(O)(OH)2. Ethephon and its 2-bromoethyl analog are more potent than its 2-fluoroethyl and thioic acid analogs and the impurities present in the tech. grade material as plant growth regulators (tomato epinasty assay), in vitro **inhibitors** of plasma **cholinesterase**, and phosphorylating agents. The biol. activity of tech. ethephon appears to be assocd. with the reactions of its principal component, particularly ethylene liberation, and possibly phosphorylating activity.

L8 ANSWER 11 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:17048 CAPLUS
DOCUMENT NUMBER: 114:17048
TITLE: Identification of the **urinary** metabolites of tacrine in the rat
AUTHOR(S): Hsu, Robert S.; Shutske, Gregory M.; Dileo, Eva M.; Chesson, Susan M.; Linville, Anastasia R.; Allen, Richard C.
CORPORATE SOURCE: Chem. Res. Dep., Hoechst-Roussel Pharm., Somerville, NJ, USA
SOURCE: Drug Metabolism and Disposition (1990), 18(5), 779-83
CODEN: DMDSAI; ISSN: 0090-9556
DOCUMENT TYPE: Journal
LANGUAGE: English
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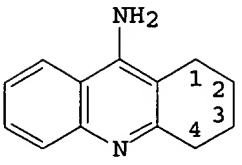


I

AB Tacrine (I, THA) is a potent **cholinesterase inhibitor** for the treatment of Alzheimer disease. The metab. and excretion of THA were studied in rats following a single oral dose of 20 mg/kg. THA was extensively metabolized. Three major **urinary** metabolites were isolated by HPLC using a semi-preparative anal. Ph column and subsequent purifn. of individual fractions on a cyano column. The major metabolic pathways involve hydroxylation of the satd. ring at positions 1,2, and 4. The structures of the metabolites 9-amino-1,2,3,4-tetrahydroacridin-1-ol (1-OH-THA), 9-amino-1,2,3,4-tetrahydroacridin-2-ol (2-OH-THA), and 9-amino-1,2,3,4-tetrahydroacridin-4-ol (4-OH-THA) were detd. by electron impact mass spectrometry and/or 1H-NMR. The **urinary** excretion of THA and metabolites was quantitated by HPLC with UV-detection. About 60% of the oral dose was eliminated as total THA, 1-OH-THA, 2-OH-THA, and 4-OH-THA over a 48-h collection interval. The non-conjugated THA and hydroxylated metabolites accounted for 45% of the dose.

L8 ANSWER 12 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:93453 CAPLUS
DOCUMENT NUMBER: 112:93453
TITLE: Action of an irreversible acetylcholine esterase **inhibitor**, soman, on muscarinic hyperpolarization in cat **bladder** parasympathetic ganglia
AUTHOR(S): Kumamoto, Eiichi; Shinnick-Gallagher, Patricia
CORPORATE SOURCE: Med. Branch, Univ. Texas, Galveston, TX, 77550, USA
SOURCE: British Journal of Pharmacology (1990), 99(1), 157-63
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Intracellular recording techniques were used to examine the action of an irreversible **acetylcholinesterase** (AChE) **inhibitor**, soman, on the hyperpolarization mediated through muscarinic cholinoceptors in cat **bladder** parasympathetic neurons. Soman (0.1-10 .mu.M) depressed the amplitude and prolonged the duration of the muscarinic slow **inhibitory** postsynaptic potential (s-i.p.s.p.) elicited by a preganglionic tetanus (40 Hz for 1 s) in the presence of mecamylamine (20 .mu.M), phentolamine (1 .mu.M) and caffeine (1 mM), in a dose-dependent manner. The effect of soman on the amplitude of the s-i.p.s.p. was partially reversible, while the effect on the duration was irreversible. Soman hyperpolarized the membrane and decreased input resistance, but this effect could not account for soman-induced inhibition of the s-i.p.s.p. Soman depressed the amplitude and prolonged the duration of a muscarinic hyperpolarization induced by pressure application of acetylcholine (ACh) in the presence of mecamylamine, phentolamine, and caffeine. The time course of this effect paralleled that on the synaptically-evoked muscarinic s-i.p.s.p. A reversible AChE **inhibitor**, pyridostigmine (10-100 .mu.M), also depressed the amplitude and prolonged the duration of a muscarinic hyperpolarization induced by either preganglionic stimulation or ACh pressure application. These actions were reversible, and not accompanied by a significant change in membrane potential or input resistance. The **inhibitory** action of soman (1 .mu.M) on the muscarinic hyperpolarization was prevented by pyridostigmine (10 .mu.M), but not by atropine (1 .mu.M). These results

demonstrate that soman prolongs not only the muscarinic hyperpolarization, but also inhibits its amplitude through a postsynaptic action, probably through AChE inhibition, in cat **bladder** parasympathetic neurons.

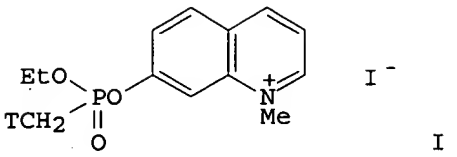
L8 ANSWER 13 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:15910 CAPLUS
DOCUMENT NUMBER: 112:15910
TITLE: Quantitative whole-body autoradiographic determination of tacrine tissue distribution in rats following intravenous or oral dose
AUTHOR(S): McNally, William; Roth, Michelle; Young, Remedios; Bockbrader, Howard; Chang, Tsun
CORPORATE SOURCE: Parke-Davis Pharm. Res., Ann Arbor, MI, 48105, USA
SOURCE: Pharmaceutical Research (1989), 6(11), 924-30, 2 plates
CODEN: PHREEB; ISSN: 0724-8741
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Tacrine (1,2,3,4-tetrahydro-9-acridinamine) has been employed in diverse clin. situations but has recently been of considerable interest for the treatment of cognitive deficits assocd. with senile dementia (Alzheimer's disease). The present studies examd. tissue distribution of radiolabeled tacrine by quant. whole-body autoradiog. Tacrine radioequivalents were widely distributed to tissue following i.v. or peroral dose, with an apparently prolonged absorption phase following the peroral dose. The presence of high levels of activity in kidneys and ureters indicates a major role for **urinary** excretion, but there is also evidence for biliary excretion and direct secretion of compd. or metabolites into the intestinal lumen. Tacrine was rapidly taken up into the brain and demonstrated regional localization to cortex, hippocampus, thalamus, and striatum. Although the inhibition of **acetylcholinesterase** by tacrine is well documented, regional uptake in brain did not correlate consistently with distribution of the enzyme, supporting suggestions by others that the alleged action of tacrine in treatment of senile dementia may be by mechanisms other than **cholinesterase** inhibition.

L8 ANSWER 14 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:585121 CAPLUS
DOCUMENT NUMBER: 109:185121
TITLE: Mechanism of action of nicotine in isolated **urinary bladder** of guinea pig
AUTHOR(S): Hisayama, Tetsuhiro; Shinkai, Michiko; Takayanagi, Issei; Toyoda, Toshie
CORPORATE SOURCE: Sch. Pharm. Sci., Toho Univ., Funabashi, 274, Japan
SOURCE: British Journal of Pharmacology (1988), 95(2), 465-72
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Nicotine produced a transient contraction of isolated strips of guinea pig **urinary bladder**. The response to nicotine was antagonized by the nicotinic receptor antagonist, hexamethonium, but was insensitive to tetrodotoxin. The nicotine-induced contraction was potentiated by the **cholinesterase inhibitor**, physostigmine, and was reduced to 50% and 70% by the muscarinic cholinoceptor antagonist, atropine, and the sympathetic neuron blocking drug, guanethidine, resp. Chem. denervation with 6-hydroxydopamine abolished the **inhibitory** effect of guanethidine. Simultaneous treatment with atropine and guanethidine did not abolish the response to nicotine, but the degree of inhibition was comparable to that obtained with atropine alone. The nicotine-induced contraction was insensitive to bunazosin and yohimbine (.alpha.1- and .alpha.2-adrenoceptor antagonists, resp.), and exogenously applied noradrenaline did not cause a contraction even in the presence of blockade of noradrenaline uptake mechanisms with

desipramine and normetanephrine and of .beta.-adrenoceptors with propranolol, suggesting a nonadrenergic nature of the sympathomimetic effect of nicotine in this tissue. The nicotine-induced contraction in the presence of atropine was abolished after desensitization of P2-purinoceptors with .alpha.,.beta.-methylene ATP, a slowly degradable ATP analog selective for P2-purinoceptors. By this desensitization, the response to ATP, but not to histamine, was also abolished. A cyclooxygenase **inhibitor**, flurbiprofen, partially inhibited the nicotine-induced contraction. The degree of the inhibition was more pronounced in the presence of atropine than in its absence. Flurbiprofen antagonized the response to exogenously applied ATP in an unsurmountable manner, but not that to carbachol. Nicotine might induce a contraction through an interaction with nicotinic receptors located on the terminals of, possibly, (1) parasympathetic cholinergic, (2) sympathetic nonadrenergic, and (3) nonsympathetic purinergic nerves in guinea pig detrusor prepns., and a portion of the contraction due to the purine nucleotide released is possibly potentiated by intramural prostaglandin(s). Parasympathetic cholinergic output might be modulated by an unknown excitatory substance released by nicotine form sympathetic nerve. Nicotine reveals a latent excitatory effect of the sympathetic hypogastric nerve which innervates guinea pig detrusor.

L8 ANSWER 15 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:217514 CAPLUS
DOCUMENT NUMBER: 108:217514
TITLE: Anticholinesterase poisonings in dogs from a cyanobacterial (blue-green algae) bloom dominated by Anabaena flos-aquae
AUTHOR(S): Mahmood, Nik A.; Carmichael, Wayne W.; Pfahler, Dave
CORPORATE SOURCE: Dep. Biol. Sci., Wright State Univ., Dayton, OH, 45435, USA
SOURCE: American Journal of Veterinary Research (1988), 49(4), 500-3
CODEN: AJVRAH; ISSN: 0002-9645
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cyanobacteria (blue-green algae) implicated in the deaths of 9 dogs at Richmond Lake, South Dakota, on August 26, 1985, were analyzed. The dominant cyanobacterial species from the water sample was A. flos-aquae. The lyophilized bloom material or the HPLC purified toxin peak, when administered to mice i.p., induced clin. signs of salivation, lacrimation, **urinary incontinence**, defecation, convulsion, fasciculation, and respiratory arrest. Further comparison of the semipurified bloom toxin with an irreversible anticholinesterase anatoxin-a(s), produced by A. flos-aquae strain NRC-525-17, revealed the bloom toxin and anatoxin-a(s) had similar properties on HPLC and on the inhibition of elec. eel **acetylcholinesterase** (EC 3.1.1.7).

L8 ANSWER 16 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:146357 CAPLUS
DOCUMENT NUMBER: 108:146357
TITLE: Tritium labeling of a powerful methylphosphonate **inhibitor** of **cholinesterase**: synthesis and biological applications
AUTHOR(S): Balan, A.; Barness, I.; Simon, G.; Levy, D.; Ashani, Y.
CORPORATE SOURCE: Israel Inst. Biol. Res., Ness-Ziona, Israel
SOURCE: Analytical Biochemistry (1988), 169(1), 95-103
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

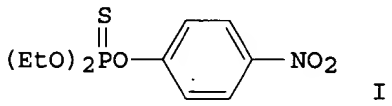
AB 7-(Methylethoxy phosphinyloxy)-1-methyl-quinolinium iodide (MEPQ), a powerful anticholinesterase methylphosphonate ester, was labeled with tritium (9 Ci/mmol) at the methylphosphonyl moiety [TCH2P(O)(OR)X] by an I-tritium replacement reaction. Kinetic measurements of the rate of inhibition of **acetylcholinesterase** (AChE) by [3H]MEPQ (I) and its rate of hydrolysis in alk. soln. confirmed the identity of I with authentic MEPQ, which was prepd. by the same reaction sequences. Gel-filtration expts. verified the radiospecificity of I. In vitro radiolabeling of both AChE and butyrylcholinesterase along with whole-body autoradiog. of I-treated mice suggests that I is a convenient marker for studying biol. systems contg. these esterases.

L8 ANSWER 17 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1987:451872 CAPLUS
DOCUMENT NUMBER: 107:51872
TITLE: Study of the ability of reversible **cholinesterase inhibitors** to bring about dissociated learning in rats
AUTHOR(S): Azarashvili, A. A.; Arkhipov, V. I.; Budantsev, A. Yu.; Prozorovskii, V. B.
CORPORATE SOURCE: Inst. Biol. Fiz., Pushchino, USSR
SOURCE: Farmakologiya i Toksikologiya (Moscow) (1987), 50(3), 27-9
CODEN: FATOAO; ISSN: 0014-8318
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB The reversible **cholinesterase inhibitors** galanthamine, eserine, and aminostigmine at 1/4-1/2 LD50 evoke a dissocd. state in rats and bring about dissocd. learning. The depression of simple, established alimentary reflexes noted during administration of large doses of reversible **inhibitors** may be lifted by administration of a mixt. of muscarinic and nicotinic cholinolytics. Ftoracizine, possing 250-fold less affinity for muscarinic receptors of the **bladder**, is only slightly inferior to atropine in its ability to lift the dissocd. state evoked by **cholinesterase inhibitors**.

L8 ANSWER 18 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1985:448697 CAPLUS
DOCUMENT NUMBER: 103:48697
TITLE: Selective facilitatory effect of vasoactive intestinal polypeptide (VIP) on muscarinic firing in vesical ganglia of the cat
AUTHOR(S): Kawatani, Masahito; Rutigliano, Michael; De Groat, William C.
CORPORATE SOURCE: Sch. Med., Univ. Pittsburgh, Pittsburgh, PA, 15261, USA
SOURCE: Brain Research (1985), 336(2), 223-34
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English
AB VIP [37221-79-7] immunoreactivity was identified in nerve fibers and in 10-13% of the neurons in pelvic and **bladder** ganglia of the cat. Ninety percent of the VIP pos. neurons contained

acetylcholinesterase [9000-81-1]. VIP immunoreactivity was not altered in decentralized ganglia 1 wk to 8 mo after transection of the pelvic and hypogastric nerves indicating that VIP fibers arose from neurons within the peripheral nervous system. The intra-arterial administration of VIP (1-50 .mu.g/kg) enhanced the postganglionic discharge elicited by the muscarinic agonist, acetyl-.beta.-methylcholine [55-92-5], but did not alter the postganglionic firing elicited by the nicotinic agonist, tetramethylammonium, or by elec. stimulation of preganglionic axons in the pelvic nerve. VIP did not elicit a postganglionic discharge in untreated ganglia, but did evoke a prolonged discharge in ganglia treated with an irreversible anticholinesterase agent, 217AO. This discharge was not affected by hexamethonium but was blocked by atropine. VIP suppressed the muscarinic inhibition of ganglionic transmission produced by acetyl-.beta.-methylcholine without altering the response to other **inhibitory** agents (norepinephrine, leucine-enkephalin, and GABA). VIP (0.1-0.3 .mu.g/kg) also had a direct **inhibitory** effect on **bladder** smooth muscle. Intraganglionic pathways contg. VIP may thus exert a selective modulatory influence on muscarinic transmission in vesical parasympathetic ganglia.

L8 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1984:204606 CAPLUS
DOCUMENT NUMBER: 100:204606
TITLE: Method for identification of **cholinesterase inhibitor** insecticides in urine
AUTHOR(S): Karakaya, Asuman
CORPORATE SOURCE: Eczacilik Fak., AU, Ankara, Turk.
SOURCE: Doga Bilim Dergisi, Seri C: Tip (1984), 8(1), 54-61
CODEN: DSTIDB; ISSN: 0254-2331
DOCUMENT TYPE: Journal
LANGUAGE: Turkish
GI



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AB A method was developed for the **urinary** identification of 25 **cholinesterase inhibitor** insecticides in cases of acute poisoning. The adsorption conditions of the insecticides on the resin and other elutions were investigated to standardize the Amberlite XAD-2 extn. method. PH 6.0-6.5 was selected as the optimum pH and at this pH value, the adsorption yields were between 74.4 and 88.7% by the spectrophotometric method. Hexane and EtOAc/1,2-dichloroethane (3:2) were selected for sequential use as elution solvents. Gas liq. chromatog. was used for recovery detns., and extn. yield for parathion (I) [56-38-2] was 80.2%. For qual. detn., the TLC-enzyme inhibition technique was standardized and the limits of sensitivity detd.

L8 ANSWER 20 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1983:400529 CAPLUS
DOCUMENT NUMBER: 99:529
TITLE: Dioxaphosphorinanes and compositions containing them
INVENTOR(S): Ashani, Yacov; Leader, Haim; Raveh, Lily; Bruckstein, Rachel; Spiegelstein, Miachel
PATENT ASSIGNEE(S): Israel Institute for Biological Research, Israel
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX

09/ 960,477

DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3220961	A1	19830217	DE 1982-3220961	19820603
DE 3220961	C2	19900517		
IL 63037	A1	19851231	IL 1981-63037	19810604
US 4472320	A	19840918	US 1982-378815	19820517

PRIORITY APPLN. INFO.: IL 1981-63037 19810604
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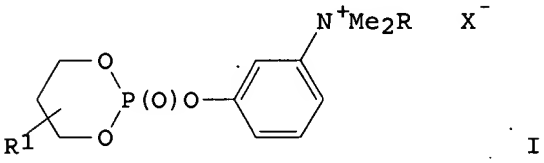

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AB The prepn. and therapeutic application of anticholinesterases, [1,3,2-dioxaphosphorinane 2-oxide derivs. I, (R = H, Me, Et, Pr, iso-Pr, Bu, iso-Bu or NR2; R1 = H or alkyl 4-, 5- or 6-position; X = physiol. compatible anion) in organophosphorus poisonings or cholinergic-assocd. diseases such as myasthenia gravis, glaucoma, or **bladder** function impairment are disclosed. Thus, O-(3-trimethylammoniumphenoxy)-1,3,2-dioxaphosphorinane 2-oxide iodide (I; R = Me; R1 = H; X = I-)(II) [80531-03-9] was prepd. by combining 2-chloro-1,3,2-dioxaphosphorinane 2-oxide [872-99-1] with 3-(dimethylamino)phenol [99-07-0] followed by addn. of MeI to the tertiary amine formed; the enzyme kinetics assocd. with the interaction of II and cholinesterases from various biol. samples as well as the protective effect of II against soman-induced **cholinesterase** inhibition in mice are given.

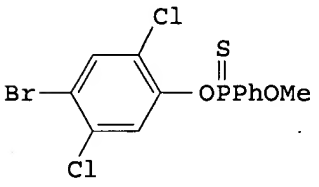
L8 ANSWER 21 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1982:593584 CAPLUS
DOCUMENT NUMBER: 97:193584
TITLE: Effects of acetylcholine on the tone and miniature contractions of isolated dog **urinary bladder**
AUTHOR(S): Mutoh, Shinji; Ueda, Shoichi; Yano, Shinjiro; Ikegami, Keiichi; Sakanashi, Matao
CORPORATE SOURCE: Med. Sch., Kumamoto Univ., Kumamoto, Japan
SOURCE: Urologia Internationalis (1982), 37(3), 183-9
CODEN: URINAC; ISSN: 0042-1138
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Incubation of both dome and trigone prepns. of dog **urinary bladder** with acetylcholine [51-84-3] produced dose-dependent increases in tone and in the frequency of miniature contractions. Both effects of acetylcholine were augmented by pretreatment of the prepns. with the **cholinesterase inhibitor** neostigmine and were depressed by the muscarinic receptor blocker atropine. The amplitude of the miniature contractions of both prepns. was not changed by acetylcholine. Changes in the tone of the **bladder** was pos. correlated with the frequency of miniature contractions. Thus, acetylcholine acts on the **urinary bladder** through activation of muscarinic receptors and changes in tone and frequency of miniature contractions are related.

L8 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1981:77883 CAPLUS
DOCUMENT NUMBER: 94:77883
TITLE: Value and use of exposure tests. XXI. The problems in improvement of information in exposure tests
AUTHOR(S): Bardodej, Z.
CORPORATE SOURCE: Lek. Fak. Hyg., Karlova Univ., Prague, Czech.
SOURCE: Cesko-Slovenska Hygiena (1980), 25(9), 440-3
CODEN: CEHYAN; ISSN: 0009-0573
DOCUMENT TYPE: Journal
LANGUAGE: Czech

AB **Urinary** tolerance limits are proposed for compds. and groups indicating exposure to aniline [62-53-3], benzene [71-43-2], ethylbenzene [100-41-4], phenol [108-95-2], fluoride, Pb, PCP [87-86-5], Hg, CS2, styrene [100-42-5], toluene [108-88-3], and trichloroethylene [79-01-6]. Indicator levels in blood are proposed for exposure to aniline, CO, methylmercury [7439-97-6], and **cholinesterase inhibitors**. The **urinary** data are based on 1.024 urine d.

L8 ANSWER 23 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1978:131655 CAPLUS
DOCUMENT NUMBER: 88:131655
TITLE: Metabolism of 14C-leptophos in the rat
AUTHOR(S): Hassan, A.; Abdel-Hamid, F. M.; Mohammed, S. I.
CORPORATE SOURCE: M. E. Reg. Radioisot. Cent., Cairo, Egypt
SOURCE: Archives of Environmental Contamination and Toxicology (1977), 6(4), 447-54
CODEN: AECTCV; ISSN: 0090-4341
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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AB The metabolic fate of leptophos (I) [21609-90-5] in the rat was investigated in vivo, using the 14C-Ph and 14C-Me-labeled insecticide. Following the administration of a single oral dose of 14C-Ph I (15 mg/kg) 46-75% of the 14C-activity was recovered after 9 days in the urine. No radioactivity was eliminated in the expired air. O-Me phenylphosphonic [10088-45-6], O-Me phenylphosphonothioic [42976-67-0] and phenylphosphonic acid [1571-33-1] were identified among the **urinary** metabolites, together with 2 metabolites of unknown nature. Demethylation of I and(or) its O analog occurred in vivo to a small extent, as confirmed by the elimination of 14CO2 in the expired air, from 14C-Me I. The insecticide seemed to accumulate in omental and s.c. fat since traces were still found in fat 12 wk after its administration. A study of the kinetics of **acetylcholinesterase** [9000-81-1] inhibition revealed that oxon [25006-32-0] was the most potent **inhibitor**. The degrdn. products were generally weak **inhibitors**.

L8 ANSWER 24 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1976:472058 CAPLUS
DOCUMENT NUMBER: 85:72058
TITLE: The effect of **cholinesterase inhibitors** on the antimuscarinic effect of hemicholinium-3 (HC-3) in the rat
AUTHOR(S): Hecker, S. E.; Mitchelson, F.
CORPORATE SOURCE: Dep. Pharmacol., Victorian Coll. Pharm., Parkville, Australia
SOURCE: Journal of Pharmacy and Pharmacology (1976), 28(5), 441-6
CODEN: JPPMAB; ISSN: 0022-3573
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hemicholinium-3 dibromide (I) [312-45-8] (1.7 .times. 10-4M) inhibited responses of the **bladder** to carbachol [51-83-2] but not to acetylcholine chloride [60-31-1]. In the presence of physostigmine sulfate [64-47-1] or diisopropyl phosphorofluoridate (II) [55-91-4] responses to acetylcholine were inhibited by I. I (2.8 .times. 10-4M) inhibited responses to both acetylcholine and carbachol in the ileum, and the degree of inhibition was not affected by any of the anticholinesterases used. I decreased the **inhibitory** action of physostigmine on the hydrolysis of acetylcholine by homogenates of rat ileum. I may interfere with the anticholinesterase activity of some **cholinesterase inhibitors** such as physostigmine and II as well as inhibiting the postjunctional muscarinic receptor.

L8 ANSWER 25 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1975:527137 CAPLUS
DOCUMENT NUMBER: 83:127137
TITLE: Effect of hepatic enzyme inducers on the in vivo and in vitro metabolism of dicrotophos, dimethoate, and phosphamidon in mice
AUTHOR(S): Tseng, Yueh-Chu L.; Menzer, Robert E.
CORPORATE SOURCE: Dep. Entomol., Univ. Maryland, College Park, MD, USA
SOURCE: Pesticide Biochemistry and Physiology (1974), 4(4), 425-37
CODEN: PCBPBS; ISSN: 0048-3575
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Daily 75 mg/kg Na phenobarbital (I) [57-30-7] i.p. injections for 3 days or 25 ppm dieldrin (II) [60-57-1] in the diet of mice for 14 days caused an increase in liver cytochrome P-450 [9035-51-2] and blood B-esterase [9016-18-6]. Liver A-esterase was not significantly increased. Under in vitro conditions, I and II induced the oxidative as well as hydrolytic metab. of dicrotophos [141-66-2], dimethoate [60-51-5], and phosphamidon [13171-21-6] by liver homogenates or combined microsomes plus 105,000g supernatant fractions. The concn. of dimethoxon [1113-02-6] was increased >4-fold by the pretreatments after incubation for 4 hr at 37.5.degree.C with NADPH added. The organophosphorus insecticides used in this study were not metabolized as well by the liver microsomes alone or 105,000g supernatant alone, as by the combination of microsomes and 105,000g supernatant. Under in vivo conditions in mice, I and II treatments increased the **urinary** recovery of metabolites in the initial 6 hr after 14C-labeled carbonyldimethoate or 14C-labeled N-ethyl-phosphamidon administration. Anal. of urine showed that the inducers caused a >6-fold increase in dimethoxon recovered and 2-fold increase in water-sol. nontoxic metabolites within 6 hr after dimethoate administration. With phosphamidon both inducers increased the rate of metab., and the total recovery in aq. and chloroform fractions was decreased. Thus, increased dimethoate toxicity after phenobarbital and

dieldrin treatments in whole animals results from stimulation of the activation of dimethoate to dimethoxon, while the increase in hydrolytic products after both pretreatments results in decreased toxicity of the direct **acetylcholinesterase inhibitors**, dicrotophos and phosphamidon.

L8 ANSWER 26 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1974:43942 CAPLUS
DOCUMENT NUMBER: 80:43942
TITLE: Response of the rat ileum, uterus, and vas deferens to carbachol and acetylcholine following repeated daily administration of a **cholinesterase inhibitor**
AUTHOR(S): Foley, D. J.; McPhillips, J. J.
CORPORATE SOURCE: Med. Cent., West Virginia Univ., Morgantown, WV, USA
SOURCE: British Journal of Pharmacology (1973), 48(3), 418-25
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Disulfoton (I) [298-04-4] (1.0 mg/kg for females, 2.5 mg/kg, i.p. for males) administered daily for 8 days produced mild to moderate signs of intoxication (tremors, **incontinence**, and diarrhea) in rats but produced no deaths. Segments of the ileum taken from the treated rats were subsensitive to carbachol [51-83-2], but the vas deferens and the uterus from these rats did not exhibit any change in sensitivity to carbachol. After I treatment, the sensitivity to acetylcholine [51-84-3] was increased in the ileum and vas deferens but not in the uterus. **Acetylcholinesterase** [9000-81-1] activity was 60-70% inhibited in all 3 tissue prepns. from I-treated animals.

L8 ANSWER 27 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1965:502415 CAPLUS
DOCUMENT NUMBER: 63:102415
ORIGINAL REFERENCE NO.: 63:18898e-f
TITLE: In vivo inhibition of rabbit whole blood **cholinesterase** following intravenous infusion of diethyl organophosphate **inhibitor** and reactivation with 2-PAM
AUTHOR(S): Shellenberger, T. E.; Bridgman, R. M.; Newell, G. W.
CORPORATE SOURCE: Stanford Res. Inst., Menlo Park, CA
SOURCE: Life Sciences (1965), 4(20), 1973-9
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Infusion of 2,2-dichloro-vinyl diethyl phosphate into rabbits for 60 min. at a rate of 0.0323 mg./min. inhibited blood **cholinesterase** to 14% of the pretreated value. An intravenous administration of pyridine-2-aldoxime methiodide (PAM) to the inhibited rabbit at 25 and 50 mg./kg. restored enzymic activity by 30 and 50%, resp., but led to a leveling off 30 min. after the injection of I. The leveling off was probably due to the **urinary** excretion of a large portion of I.

L8 ANSWER 28 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1964:495418 CAPLUS
DOCUMENT NUMBER: 61:95418
ORIGINAL REFERENCE NO.: 61:16631a-d
TITLE: Effect of anticholinesterases, atropine, and PAM-4 on isolated smooth muscle preparations with autonomic nervous supply from mice and rats. Isolated **urinary bladder** and vas deferens with nerve supply
AUTHOR(S): Hukovic, S.; Bubic, I.
CORPORATE SOURCE: Med. School, Univ. Sarajevo, Yugoslavia

09/ 960,477

SOURCE: Acta Med. Iugoslav. (1963), 17(3), 300-20
DOCUMENT TYPE: Journal
LANGUAGE: Croatian

AB The prepn. of the isolated **urinary** rat **bladder** with the parasympathetic pelvic nerve, and of the vas deferens with the sympathetic hypogastric nerve is described. Nerve stimulations produced contractions that could be repeated every min. for more than 2 hrs. without appreciable decrease. There were no spontaneous contractions. Anticholinesterases (I) increased the stimulatory effect in both prepns., being 50-100-fold more potent in the vas deferens. Both prepns. were resistant to atropine (II). The resistance to II diminished when it was added after **cholinesterase** (III) poisons. II blocked stimulation of the **urinary bladder** and largely decreased it on the vas deferens in the 1st 2-3 min., diminishing functional antagonism. Hexamethonium produced no blocking effect, but increased stimulation in the **bladder**, as did acetylcholine after II was given. When I was given, 1st in low concns. and then in progressively greater concns., there were no strong reactions. The effect was similar to that when II was given previously. When III was inhibited, the **bladder** showed a spasmolytic effect. PAM-4 increased the effect of sympathetic stimulation and decreased that of parasympathetic stimulation, an effect similar to that produced by noradrenaline. PAM-4 contributed to the functional antagonism. It was assumed that the functional adaptation to the III poisons was due to the spasmolytic effect of I when III was inhibited. Many factors should be controlled in I intoxications besides the III inhibition, the most important being the decrease of functional antagonism after II and the spasmolytic effect of III poisons when the enzyme is inhibited.

L8 ANSWER 29 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1964:477846 CAPLUS
DOCUMENT NUMBER: 61:77846
ORIGINAL REFERENCE NO.: 61:13601e-h,13602a
TITLE: Effect of a tranquilizer on pituitary and adrenocortical activity
AUTHOR(S): Fujimoto, Y.
CORPORATE SOURCE: Univ. Tokyo
SOURCE: Nippon Geka Gakkai Zasshi (1959), 60(5), 759-75
CODEN: NGGZAK; ISSN: 0301-4894
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The effect of tranquilization on pituitary-adrenocortical activity was investigated by analyzing the ascorbic acid content of rat adrenal glands, circulating eosinophils, plasma 17-hydroxy corticosteroids (I) levels, and **urinary** excretion of corticoids in both patients and dogs, and the amt. of I in the adrenal venous blood of dogs. Chlorpromazine (II) per se caused adrenal ascorbic acid depletion, elevation of the plasma I level, increased secretion of corticoids into the adrenal venous blood, and a decrease in circulating eosinophils. The leukocyte count also decreased temporarily, but a rebound increase was noted after 3-4 hrs., despite the continuing fall of the eosinophil count. Gomori-pos. substance decreased markedly immediately after intravenous injection of II. Adrenal ascorbic acid depletion after II administration did not occur in hypophysectomized rats. The intramuscular injection of 0.5 mg./100 g. of II in rats blocked the adrenal ascorbic acid depletion caused by unilateral adrenalectomy, but not that caused by manipulation of the intestines or by hemorrhage. Administered intravenously, it effectively inhibited the response to such surgical attack, but caused also acute collapse in almost every rat. In 5 patients operated on under artificial tranquilization, the circulating eosinophil count, **urinary** excretion of corticoids, and blood sugar level were similar to those in 8 patients operated on under anesthesia without II. However, the increase in plasma I and serum **cholinesterase** 4-8 hrs. after surgery was less extreme in the

former group. II did not significantly inhibit the increase in I in the adrenal venous blood of dogs after adrenal vein cannulation, a moderately severe surgical attack. The **inhibitory** effect of II was found, by detns. of neurosecretions and action currents in dogs, to occur at the level of the hypothalamus and pituitary gland. Exogenous ACTH caused a marked decrease in the adrenal ascorbic acid content in rats which had been given enough II to inhibit the response to stress. In hypothermia with or without II, the pituitary-adrenocortical activity was decreased, and response to surgical aggression was also strongly depressed. II did not affect the half-life of administered hydrocortisone. In hypothermia, conjugation of free I in the liver was presumed to be retarded. From Abstr. Japan. Med. 1(7), Abstr. No. 2706(1961).

L8 ANSWER 30 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1964:477845 CAPLUS
DOCUMENT NUMBER: 61:77845
ORIGINAL REFERENCE NO.: 61:13601e-h,13602a
TITLE: Effect of a tranquilizer on pituitary and adrenocortical activity
AUTHOR(S): Fujimoto, Y.
CORPORATE SOURCE: Univ. Tokyo
SOURCE: Nippon Geka Gakkai Zasshi (1959), 60(4), 640-62,759-75
CODEN: NGGZAK; ISSN: 0301-4894
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The effect of tranquilization on pituitary-adrenocortical activity was investigated by analyzing the ascorbic acid content of rat adrenal glands, circulating eosinophils, plasma 17-hydroxy corticosteroids (I) levels, and **urinary** excretion of corticoids in both patients and dogs, and the amt. of I in the adrenal venous blood of dogs. Chlorpromazine (II) per se caused adrenal ascorbic acid depletion, elevation of the plasma I level, increased secretion of corticoids into the adrenal venous blood, and a decrease in circulating eosinophils. The leukocyte count also decreased temporarily, but a rebound increase was noted after 3-4 hrs., despite the continuing fall of the eosinophil count. Gomori-pos. substance decreased markedly immediately after intravenous injection of II. Adrenal ascorbic acid depletion after II administration did not occur in hypophysectomized rats. The intramuscular injection of 0.5 mg./100 g. of II in rats blocked the adrenal ascorbic acid depletion caused by unilateral adrenalectomy, but not that caused by manipulation of the intestines or by hemorrhage. Administered intravenously, it effectively inhibited the response to such surgical attack, but caused also acute collapse in almost every rat. In 5 patients operated on under artificial tranquilization, the circulating eosinophil count, **urinary** excretion of corticoids, and blood sugar level were similar to those in 8 patients operated on under anesthesia without II. However, the increase in plasma I and serum **cholinesterase** 4-8 hrs. after surgery was less extreme in the former group. II did not significantly inhibit the increase in I in the adrenal venous blood of dogs after adrenal vein cannulation, a moderately severe surgical attack. The **inhibitory** effect of II was found, by detns. of neurosecretions and action currents in dogs, to occur at the level of the hypothalamus and pituitary gland. Exogenous ACTH caused a marked decrease in the adrenal ascorbic acid content in rats which had been given enough II to inhibit the response to stress. In hypothermia with or without II, the pituitary-adrenocortical activity was decreased, and response to surgical aggression was also strongly depressed. II did not affect the half-life of administered hydrocortisone. In hypothermia, conjugation of free I in the liver was presumed to be retarded. From Abstr. Japan. Med. 1(7), Abstr. No. 2706(1961).

L8 ANSWER 31 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1964:63161 CAPLUS
DOCUMENT NUMBER: 60:63161

09/ 960,477

ORIGINAL REFERENCE NO.: 60:11149f-g
TITLE: The role of adrenal cortex and of some blood enzymes in normal and pathologic parturition
AUTHOR(S): Anastas'eva, N. V.; Grosblat, R. Sh.
SOURCE: Nauchn. Zap. Uzhgorodsk. Univ. (1962), 47, 8-12 From: Ref. Zh. Khim., Biol. Khim. 1962, Abstr. No. 24S1577.
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Activities of pitocinase (I), **cholinesterase** (II) and antihyaluronidase (III) were high during normal parturition. Excretion of 17-keto steroid (IV) during and shortly after delivery was 4.8-6.8 mg. in 24 hrs. Frequent cases were noted in which blood sugar decreased and Na and chlorides rose during delivery, Ca and K returned to normal, and activity of I and II dropped. In women with premature flow of placental water, only III fell to lower levels. Blood sugar, Na, chlorides, and I and II activity fell to lower levels and excretion of IV was reduced to 1.4-2.5 mg. per 24 hrs. in cases with primary delivery weakness, while in some cases K concn. was increased.

L8 ANSWER 32 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1961:8478 CAPLUS
DOCUMENT NUMBER: 55:8478
ORIGINAL REFERENCE NO.: 55:1737d-f
TITLE: Experimental-biological basis for maximum tolerances of radioactive isotopes entering an organism
AUTHOR(S): Durmish'yan, M. G.
SOURCE: Trudy Vsesoyuz. Nauch.-Tekh. Konf. po Primenen. Radioaktiv. i Stabil. Isotopov i Izluchenii v Narod. Khoz. i Nauke, Med. Radiobiol., Moscow (1960), Volume Date 1957 345-59
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The rate of elimination of Na24 varies irregularly with the dosage given to rats. A subthreshold dose of unspecified chem. irritants given along with Na24 may repress blood **cholinesterase** for prolonged periods, whereas either substance alone produces no such change, indicating a synergistic action of nonradioactive compds. on the action of radioisotopes within the organism. The blood-forming system in rabbits is very sensitive to Na24 as are the adrenals. The threshold dose of Na24 is estd. at 0.25 mc. for the most sensitive functions of skin permeability and stimulation of leucocytes and reticulocytes in rabbits; in rats the thresholds of most sensitive functions (adrenocortical function and renal absorption) are 0.01 mc., while conditioned reflex function has the threshold level of 0.005-0.01. In dogs the **urinary** function has a threshold of 1 mc. of Na24.

L8 ANSWER 33 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1960:18520 CAPLUS
DOCUMENT NUMBER: 54:18520
ORIGINAL REFERENCE NO.: 54:3727h-i,3728a-c
TITLE: Pharmacological studies of cyclanoline and steponine, the quarternary ammonium alkaloids isolated from menispermacous plants. I
AUTHOR(S): Oyaizu, Susumu
CORPORATE SOURCE: Kyoto Univ.
SOURCE: Breviaria (1958), 50,
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cyclanoline (I) and steponine (II) were isolated from Cyclea insularis and Stephania japonica, resp. I was found to have a muscle-relaxant effect on the sciatic-gastrocnemius prepn. of rat in situ and the intensity of the effect was about 1/10 that of menisperine, an alkaloid from Menispermum

dauricum. The muscle-relaxant activity of I resembled that of d-tubocurarine and was antagonized by such **cholinesterase inhibitors** as eserine and prostigmine. I showed a contractile effect on the rectus abdominis muscle of frog in vitro. II caused no such action but potentiated the contractile action of acetylcholine in low concns. I and II in high concns. inhibited the contractile response of the prepn. to acetylcholine. I and II showed a hypotensive action which was mainly due to the blocking action on the sympathetic ganglia. I and II inhibited or abolished the contractile response of the nictitating membrane of cat to cervical sympathetic stimulation, the hypertensive response to splanchnic nerve stimulation in dog, the hypotensive response to vagal stimulation in cat, the contractile response of the stomach in rabbit, the contractile response of the **bladder** to pelvic nerve stimulation in cat, and the salivatory response to chorda tympani stimulation in dog. I and II showed muscarinic action on the intestine of rabbit in vitro and also in vivo, and on the perfused vessels of rabbit's ear. Both drugs had considerable nicotinolytic action on the intestine of rabbit in vitro and in vivo, on the isolated heart, on the blood pressure, and on the nictitating membrane in cat. I and II slightly inhibited the gastric secretion in Shay rats. Av. L.D.50 in mouse intraperitoneally was 0.79 mg./10 g. for II and 0.68 for I; the value for menisperine was 0.11.

L8 ANSWER 34 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1960:18519 CAPLUS
DOCUMENT NUMBER: 54:18519
ORIGINAL REFERENCE NO.: 54:3727h-i,3728a-c
TITLE: Pharmacological studies of cyclanoline and steponine, the quarternary ammonium alkaloids isolated from menispermacous plants. I
AUTHOR(S): Oyaizu, Susumu
CORPORATE SOURCE: Kyoto Univ.
SOURCE: Nippon Yakurigaku Zasshi (1958), 54, 1093-105
CODEN: NYKZAU; ISSN: 0015-5691
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Cyclanoline (I) and steponine (II) were isolated from Cyclea insularis and Stephania japonica, resp. I was found to have a muscle-relaxant effect on the sciatic-gastrocnemius prepn. of rat in situ and the intensity of the effect was about 1/10 that of menisperine, an alkaloid from Menispermum dauricum. The muscle-relaxant activity of I resembled that of d-tubocurarine and was antagonized by such **cholinesterase inhibitors** as eserine and prostigmine. I showed a contractile effect on the rectus abdominis muscle of frog in vitro. II caused no such action but potentiated the contractile action of acetylcholine in low concns. I and II in high concns. inhibited the contractile response of the prepn. to acetylcholine. I and II showed a hypotensive action which was mainly due to the blocking action on the sympathetic ganglia. I and II inhibited or abolished the contractile response of the nictitating membrane of cat to cervical sympathetic stimulation, the hypertensive response to splanchnic nerve stimulation in dog, the hypotensive response to vagal stimulation in cat, the contractile response of the stomach in rabbit, the contractile response of the **bladder** to pelvic nerve stimulation in cat, and the salivatory response to chorda tympani stimulation in dog. I and II showed muscarinic action on the intestine of rabbit in vitro and also in vivo, and on the perfused vessels of rabbit's ear. Both drugs had considerable nicotinolytic action on the intestine of rabbit in vitro and in vivo, on the isolated heart, on the blood pressure, and on the nictitating membrane in cat. I and II slightly inhibited the gastric secretion in Shay rats. Av. L.D.50 in mouse intraperitoneally was 0.79 mg./10 g. for II and 0.68 for I; the value for menisperine was 0.11.

L8 ANSWER 35 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1957:22197 CAPLUS

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DOCUMENT NUMBER: 51:22197
ORIGINAL REFERENCE NO.: 51:4485g-i
TITLE: Inhibition of serum **cholinesterase** by lysergic acid derivatives. Submicrodetection of lysergic acid diethylamide
AUTHOR(S): Goldenberg, Harry; Goldenberg, Vivian
CORPORATE SOURCE: Hillside Hosp., Glen Oaks, NY
SOURCE: J. Hillside Hosp. (1956), 5, 246-57
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB A semiquant. method for the detection of D-lysergic acid diethylamide (LSD) based on the inhibition of serum **cholinesterase** is described. In the absence of interferences, the procedure can be used to detect as little as 0.2 .gamma. of LSD. **Urinary** LSD was extd. from alk. medium with ethylene dichloride, reextd. with acid, extd. into a small vol. of ethylene dichloride, and taken to dryness. Hestrin's (C.A. 44, 77f) colorimetric method for serum **cholinesterase** activity was used for detn. of inhibition by LSD and its derivs. Recovery of LSD from urine was approx. 50%. The relative **inhibitory** activity of LSD, related compds., and known **inhibitors** of serum **cholinesterase** follows the order: eserine > LSD > D-2-bromo-LSD > prostigmine > D-lysergic acid monoethylamide > chlorpromazine > serotonin = tryptamine > mescaline.

L8 ANSWER 36 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1956:2134 CAPLUS
DOCUMENT NUMBER: 50:2134
ORIGINAL REFERENCE NO.: 50:465d-f
TITLE: Type and distribution of cholinesterases of **urinary** collecting system of dogs: their relation to ureteral peristalsis and possible role in congenital anomalies
AUTHOR(S): de Klerk, Johan N.
CORPORATE SOURCE: Johns Hopkins Hosp., Baltimore, MD
SOURCE: Journal d'Urologie Medicale et Chirurgicale (1954), 72, 787-98
CODEN: JUMCAZ; ISSN: 0368-4679
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The pelvi-ureteral musculature of the dog contains a **cholinesterase** (I) alone. There is no evidence of **acetylcholinesterase** activity in these tissues. This observation is also established for the trigone of the **bladder**. The remainder of the **bladder** musculature exhibits a predominant **acetylcholinesterase** activity and a min. evidence of I activity. The I of the dog ureter can be inhibited in vivo by the passage of diisopropyl fluophosphate 10-6M soln. through the lumen. Inhibition of the I of the dog ureter results in cessation of ureteral peristalsis and increased ureteral tone. Evidence is presented which suggests the existence of a I **inhibitor** in the urine of the normal dog. The implications of these findings and their possible role in the normal ureteral peristalsis are discussed. The possible role of the acetylcholine metabolic cycle in the pathogenesis of the **urinary** collecting system is discussed.

L8 ANSWER 37 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1954:47002 CAPLUS
DOCUMENT NUMBER: 48:47002
ORIGINAL REFERENCE NO.: 48:8365b-c
TITLE: Seasonal variation of the amount of creatinine in urine
AUTHOR(S): Fukuyama, Tomitaro
CORPORATE SOURCE: Public Hyg. Inst., Tokyo

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SOURCE: Nisshin Igaku (1952), 39, 200-7
CODEN: NIIGAL; ISSN: 0369-4143
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 45, 6681e. Concn. of creatinine in **urinary** excretion increased in summer, max. 1.22-1.81 g./day in July, and decreased in winter, min. 0.91-1.13 g./day. Though the activity of **cholinesterase** decreased in summer, inactivation of it in winter with the injection of an **inhibitor** did not increase the amt. of creatinine excreted.

L8 ANSWER 38 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1948:10723 CAPLUS
DOCUMENT NUMBER: 42:10723
ORIGINAL REFERENCE NO.: 42:2348f-h
TITLE: Diisopropyl fluorophosphate (DFP) and **cholinesterase**
AUTHOR(S): Heymans, C.; Jacob, J.
CORPORATE SOURCE: Univ. Gand, Belg.
SOURCE: Archives Internationales de Pharmacodynamie et de Therapie (1947), 74, 233-52
CODEN: AIPTAK; ISSN: 0003-9780
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Diisopropyl fluorophosphate (5 mg./kg.) in nonanesthetized dogs produces convulsions, muscle twitchings, bronchospasm, hyperperistalsis and **bladder** contractions but no increased blood pressure or change of heart rate. Larger doses slow the heart. Atropine suppresses the effects except the convulsions and muscle twitchings. Nembutal decreases the convulsions. The muscle twitchings persist in denervated muscle but do not occur after axon degeneration. Injection of DFP into the perfused dog head does not increase the direct or reflex excitability of the cardio-**inhibitory** vagal and respiratory centers.

L8 ANSWER 39 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1947:22745 CAPLUS
DOCUMENT NUMBER: 41:22745
ORIGINAL REFERENCE NO.: 41:4563f-i
TITLE: Acetylcholine shock
AUTHOR(S): Danielopolu, D.
SOURCE: Acta Medica Scandinavica (1947), 126, 595-601
CODEN: AMSVAZ; ISSN: 0001-6101
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Acetylcholine (ACh) shock is an acute condition characterized by hyperfunction of organs in which parasympathin (P) is the excitor and sympathin (S) the **inhibitor** or by hypfunction of organs where P is the **inhibitor** and S the excitor. The symptoms include bradycardia, A-V block, hypotension, hypothermy, hypermotility of the digestive tract, uterus, or **bladder**, bronchial constriction, convulsions, leucopenia with mononucleosis and eosinophilia. The shock may be transitory or may end in death. It is assocd. with an increased production or with a decreased destruction of ACh. This type of shock can be provoked by intravenous injections of ACh. It can be prevented with atropine. In the atropinized animal ACh has a sympathomimetic action causing hypertension. A similar shock can be provoked by stimulating the peripheral end of the vagus whereby over-production of ACh is effected. Asthma is due to ACh shock. The disease is assocd. with a localized parasympathetic preponderance. Similarly, sea sickness is a generalized ACh shock caused reflexly through the vestibular organ and can be forestalled with atropine. ACh shock also can be produced by decreased destruction; for instance, by the aid of eserine, but this action is very complicated because of the adrenosecretory action of the eserine.

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Intoxication by digitalis or strophanthin is also due largely to ACh since they inactivate **cholinesterase**. The protective mechanisms which the organism can release against ACh shock are discussed.

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FILE 'CAPLUS' ENTERED AT 17:49:18 ON 27 JUN 2003

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L1          387 S (ACETYLCHOLINESTERASE OR CHOLINESTERASE) AND (URINARY OR BLAD
L2            2 S L1 AND PYRROLO
L3          385 S L1 NOT L2
L4          345 S L3 NOT PY>1998
L5            1 S L4 AND (TRICYCLIC OR TRICYCLE?)
L6          344 S L4 NOT L5
L7          328 S L6 NOT PY>1997
L8           39 S L7 AND INHIBITOR?
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